

WIDEPOINT CORP
Form DEF 14A
October 30, 2015

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, DC 20549

SCHEDULE 14A

(RULE 14a-101)

SCHEDULE 14A INFORMATION

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

Exchange Act of 1934 (Amendment No. _____)

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

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

WidePoint Corporation
(Name of Registrant as Specified in its Charter)

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

Payment of Filing Fee (Check the appropriate box):

No fee required.

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

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

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(4) Proposed maximum aggregate value of transaction:

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(1) Amount Previously Paid:

(2) Form, Schedule or Registration Statement No.:

(3) Filing Party:

(4) Date Filed:

WIDEPOINT CORPORATION

7926 Jones Branch Drive, Suite 520

McLean, Virginia 22102

October 30, 2015

To Our Stockholders:

You are cordially invited to attend the Annual Meeting of Stockholders of WidePoint Corporation, which will be held at 10:00 a.m., EST, on Thursday, December 17, 2015 at the Washington, D.C. offices of Foley & Lardner LLP, located at 3000 K Street N.W., Sixth Floor, Washington, D.C. 20007.

The accompanying notice of meeting and proxy statement describe the matters to be voted on at the meeting.

YOUR VOTE IS IMPORTANT. We invite you to attend the meeting in person. If attending the meeting is not feasible, we encourage you to read the proxy statement and vote your shares as soon as possible. To ensure your shares will be represented, we ask that you vote your shares via the Internet or by telephone, as instructed on the Notice of Internet Availability of Proxy Materials or as instructed on the accompanying proxy. If you received or requested a copy of the proxy card by mail, you may submit your vote by completing, signing, dating and returning the proxy card by mail. We encourage you to vote via the Internet or by telephone. These methods save us significant postage and processing charges. Please vote your shares as soon as possible. This is your Annual Meeting and your participation is important.

Sincerely,

S.L. Komar

Steve L. Komar
Chairman of the Board, President and
Chief Executive Officer

WIDEPOINT CORPORATION

7926 Jones Branch Drive, Suite 520

McLean, Virginia 22102

NOTICE OF 2015 ANNUAL MEETING OF STOCKHOLDERS

The Annual Meeting of Stockholders of WidePoint Corporation will be held on Thursday, December 17, 2015 at 10:00 a.m., EST, at the Washington, D.C. offices of Foley & Lardner LLP, located at 3000 K Street, N.W., Sixth Floor, Washington, D.C. 20007 to consider and vote on the following matters described in the accompanying proxy statement:

To elect the three director nominees named in the attached proxy statement as Class III directors to serve for a three-year period until the Annual Meeting of Stockholders in the year 2018 and to elect the one director nominee named in the attached proxy statement as a Class I director to serve until the Annual Meeting of Stockholders in the year 2016;

To ratify the selection of Moss Adams LLP as the Company's independent accountants; and

To transact such other business as may properly come before the meeting.

Stockholders of record at the close of business on October 23, 2015 are entitled to receive notice of, and to vote in person or by proxy at, the Annual Meeting.

By order of the Board of Directors,

J.T. McCubbin

James T. McCubbin
Corporate Secretary

October 30, 2015

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WIDEPOINT CORPORATION

7926 Jones Branch Drive, Suite 520

McLean, Virginia 22102

PROXY STATEMENT

This Proxy Statement is furnished in connection with the solicitation by the Board of Directors of WidePoint Corporation, a Delaware corporation (referred to herein as “WidePoint,” the “Company,” “we” or “our”), of proxies of stockholders to be voted at the 2015 WidePoint Annual Meeting of Stockholders to be held at the Washington, D.C. offices of Foley & Lardner LLP, located at 3000 K Street, N.W., Sixth Floor, Washington, D.C. 20007 at 10:00 a.m., EST, on Thursday, December 17, 2015, and any and all adjournments thereof.

Any stockholder executing a proxy retains the right to revoke it at any time prior to its being exercised by giving written notice to the Secretary of the Company.

This Proxy Statement and the accompanying proxy are first being sent to stockholders of the Company on or about October 30, 2015.

Notice of Electronic Availability of Proxy Materials

In accordance with regulations adopted by the Securities and Exchange Commission, instead of mailing a printed copy of our proxy materials, including our annual report to stockholders, to each stockholder of record, we may now furnish these materials by mail or e-mail. On or about October 30, 2015, we mailed to our stockholders who have not previously requested to receive these materials by mail or e-mail a Notice of Internet Availability of Proxy Materials containing instructions on how to access this proxy statement and our annual report and to vote online. The Notice instructs you as to how you may access and review all of the important information contained in the proxy materials. The Notice also instructs you as to how you may submit your proxy on the Internet or by telephone. If you received the Notice by mail, you will not automatically receive a printed copy of our proxy materials or annual report unless you follow the instructions for requesting these materials included in the Notice. For directions to the Annual Meeting, please contact James McCubbin at jmccubbin@widepoint.com or at (703) 349-2577.

Voting Procedures and Securities

Your Vote is Very Important

Whether or not you plan to attend the meeting, please take the time to vote your shares as soon as possible. You may submit your vote by completing, signing, dating and returning the proxy card by mail. We encourage you to vote via the Internet or by telephone. These methods save us significant postage and processing charges.

Vote Required, Abstentions and Broker Non-Votes

Shares of WidePoint common stock represented by proxy will be voted according to the instructions, if any, given in the proxy. Unless otherwise instructed, the person or persons named in the proxy will vote (1) FOR the election of the nominees for director listed herein (or a substitute in the event any of the nominees are unavailable for election); (2) FOR the ratification of the selection of Moss Adams LLP as the independent accountants for the Company for the current fiscal year; and (3) in their discretion, with respect to such other business as may properly come before the meeting. The Board of Directors has designated Steve L. Komar and James T. McCubbin, and each or any of them, as proxies to vote the shares of common stock solicited on its behalf.

Votes cast by proxy or in person at the Annual Meeting will be tabulated by an inspector of election appointed by the Company for the meeting. A quorum of stockholders is necessary to hold a valid meeting. A quorum will be present if at least a majority of the outstanding shares of common stock of the Company entitled to vote are present at the Annual Meeting in person or by proxy. A director is elected by a plurality of the votes cast at the Annual Meeting, which means that the nominees who receive the highest number of properly executed votes will be elected as a director, even if that nominee did not receive a majority of the votes cast. The ratification of the appointment of Moss Adams LLP as the Company's independent accountants requires the affirmative vote of the majority of the votes present, in person or by proxy, and voting at the Annual Meeting.

The inspector of election will treat abstentions as shares that are present and entitled to vote for purposes of determining the presence of a quorum, but as unvoted for purposes of determining the approval of any matter submitted to the stockholders for a vote. Your broker, bank or other nominee is permitted to vote your shares on the ratification of the appointment of Moss Adams LLP as our independent auditor without receiving voting instructions from you. All other items are "non-discretionary" items. This means brokerage firms that have not received voting instructions from their clients on any proposal other than the appointment of Moss Adams LLP will not be permitted to vote such shares for any other matters at the Annual Meeting. These "broker non-votes" will be included in the calculation of the number of votes considered to be present at the Annual Meeting for purposes of determining a quorum, but will not be considered in determining the number of votes necessary for approval and will have no effect on the outcome of any of the proposals because in tabulating the voting results, shares that constitute broker non-votes are not considered votes cast on that proposal.

The cost of soliciting proxies will be borne by the Company. Certain of our officers and other employees may, without compensation other than their regular compensation, solicit proxies by further mailing or personal conversations, or by telephone, facsimile or other electronic means. We will also, upon request, reimburse brokers and other persons holding stock in their names, or in the names of nominees, for their reasonable out-of-pocket expenses for forwarding proxy materials to the beneficial owners of our stock and to obtain proxies.

Shares Outstanding

As of October 23, 2015, the record date for determining stockholders entitled to vote at the Annual Meeting, a total of 82,520,696 shares of common stock of the Company, par value \$.001 per share, which is the only class of voting securities of the Company, were issued and outstanding. All holders of record of the common stock as of the close of business on October 23, 2015 are entitled to one vote for each share held when voting at the Annual Meeting, or any adjournment thereof, upon the matters listed in the Notice of Annual Meeting. Cumulative voting is not permitted.

Other Business

The Board knows of no other matters to be presented for stockholder action at the meeting. If other matters are properly brought before the meeting, the persons named as proxies in the accompanying proxy card intend to vote the shares represented by them in accordance with their best judgment.

Proposal One – Election of Directors

The Company's Board is classified into three classes of directors, with one class of directors being elected at each annual meeting of stockholders of the Company to serve for a term of three years or until the earlier expiration of the term of their class of directors or until their successors are elected and take office as provided below. To maintain the staggered terms of election of directors, stockholders of the Company are voting upon the election of three Class III directors to serve for a three-year period until the 2018 Annual Meeting of Stockholders and one Class I director to serve until the 2016 Annual Meeting of Stockholders.

The Bylaws of the Company provide that the Board will determine the number of directors to serve on the Board. The Company's Board presently consists of six members and there is a director vacancy in Class I. The Board, upon the recommendation of the Corporate Governance and Nominating Committee, has nominated Paul Johnson for election to the Board as a director to fill the vacancy in Class I. All other director nominees are currently serving as members of the Board.

Proxies will be voted at the Annual Meeting, unless authority is withheld, FOR the election of the persons named below. The Company does not contemplate that the persons named below will be unable or will decline to serve; however, if such nominee is unable or declines to serve, the persons named in the accompanying proxy will vote for a substitute, or substitutes, in their discretion.

Class III Director Nominees For a Term That Will Expire at the 2018 Annual Meeting of Stockholders:

Name	Age	Position
James Ritter	71	Director, Chairman of the Compensation and Corporate Governance and Nominating Committees
Otto Guenther	74	Director
George Norwood	73	Director

James M. Ritter has served as a director since December 1999 and served as Assistant Secretary of the Company from December 2002 until 2008. Mr. Ritter is the Chairman of the Corporate Governance and Nominating Committee and the Compensation Committee and is also a member of the Audit Committee. Mr. Ritter is the retired Corporate Headquarters Chief Information Officer of Lockheed Martin Corporation. Prior to his retirement in February 2001, Mr. Ritter was employed at Lockheed Martin Corporation for over 32 years in various positions involving high level IT strategic planning and implementation, e-commerce development, integrated financial systems, and large-scale

distributed systems.

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Mr. Ritter brings to the Board extensive knowledge of information systems and managerial experience as a result of a career managing and building complex information technology systems. This experience, as well as his independence from the Company, his prior performance as a Board member led the Board to conclude that he should continue to serve as a director of the Company.

Lieutenant General (Ret.) Otto J. Guenther has served as a director since his appointment on August 15, 2007. General Guenther serves as a member of the Corporate Governance and Nominating Committee. He joined the Board after a distinguished 34-year military career, including serving as the Army's first chief information officer, followed by nearly a decade of exceptional leadership within the federal information technology industry. His key assignments included the following: commanding general for Fort Monmouth, NJ, and the Communications Electronics Command; program executive officer for the Army's tactical communications equipment; project manager for the Tactical Automated Data Distribution System; and commander for the Defense Federal Acquisition Regulatory Council. General Guenther recently retired from Northrop Grumman Mission Systems, where he served as the Sector Vice President and General Manager of Tactical Systems Division. While there, he oversaw battlefield digitization, command and control, and system engineering activities for the U.S. Army. Under his leadership, the division grew to approximately 1,650 employees across several locations and completed over \$700 million in acquisitions. Previously General Guenther was general manager of Computer Associates International's Federal Systems Group, a \$300 million operation providing IT products and services to the federal market area. General Guenther was awarded several honors by the U.S. Army, including the Distinguished Service Medal, Legion of Merit (Oak Leaf Cluster), Defense Superior Service Medal (Oak Leaf Cluster), Joint Service Medal, and Army Commendation Medal. Recognized for his work within the industry, he also received several Armed Forces Communications and Electronics Association awards and was inducted into the Government Computer News Hall of Fame. Currently, General Guenther sits on two educational foundations, AFCEA Education Foundation and Aurora Foundation, and since 2006 has been an active trustee at McDaniel College. General Guenther received a Bachelor of Science Degree in Economics from Western Maryland College, now called McDaniel College, and a Master's Degree in Procurement and Contracting from the Florida Institute of Technology.

General Guenther brings to the Board extensive knowledge of the federal marketplace as a result of a career that has spanned both military and informational technology industries. In addition, General Guenther's knowledge of federal infrastructure as well as experience in successful business development and board service is particularly valuable to the Company. This experience, as well as his independence from the Company and his prior performance as a Board member, led the Board to conclude that he should continue to serve as a director of the Company.

Major General (Ret.) George W. Norwood has served as a director since his appointment on August 15, 2007. General Norwood serves as a member of the Audit Committee and the Compensation Committee. General Norwood also currently serves on the board of directors of Scalable Network Technologies. He is also on the boards of advisors of Peduzzi Associates, Ltd., AtHoc, Inc. and Airborne Tactical Advantage Company. General Norwood brings to the Board extensive knowledge of the federal marketplace as a result of a distinguished 30-year military career and more than 12-years in the commercial market with significant experience in both military and defense contracting.

General Norwood is currently President and Chief Executive Officer of Norwood & Associates, Inc. of Tampa, Fla., which maintains extensive international and U.S. networks of government, military and private sector contacts while providing technical and strategic planning expertise to corporations pursuing defense-related opportunities. General Norwood previously served as Deputy Chief of Staff for the United Nations Command and United States Forces in Korea from 1995 to 1997. He also served as the U.S. member of the United Nations Command's Military Armistice Commission responsible for crucial general officer level negotiations with North Korea.

General Norwood received a Bachelor of Science Degree in Mathematics from San Diego State University and a Master's Degree in Business Administration from Golden Gate University. He is also a graduate of the National War College and Defense Language Institute.

General Norwood's experience supporting the federal infrastructure as well as his experience in successful business development and board service is particularly valuable to the Company. This experience, as well as his independence from the Company and his prior performance as a Board member, led the Board to conclude that he should continue to serve as a director of the Company.

Class I Director Nominee For a Term That Will Expire at the 2016 Annual Meeting of Stockholders:

Name	Age	Position
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Paul Johnson	54	Director Nominee
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Paul Johnson is a nominee for director. Since its inception in 2012, Mr. Johnson has managed Nicusa Investment Advisors, a firm focused on advising senior management and boards of directors on governance, strategy, capital allocation, and shareholder value creation. Mr. Johnson is also a senior advisor to Bowen Advisors, an organization focused on offering M&A and strategic advisory services to emerging and high growth technology firms. Prior to the inception of Nicusa Investment Advisors in 2012, Mr. Johnson was the general partner and investment manager of Nicusa Capital Partners, a private investment partnership that he started in 2003, which invested in virtually all sectors of the economy, with a concentration in technology. Prior to founding Nicusa, Mr. Johnson was a Managing Director

in the Equity Research Department of Robertson Stephens, where he worked from 1994 through 2002. Mr. Johnson has been an Adjunct Professor of Finance at the Graduate School of Business, Columbia University, since 1992, where he teaches courses on securities analysis and value investing. Mr. Johnson was appointed as a Fellow to the Gabelli Center for Global Security Analysis at Fordham University in August 2015 and will teach an introductory class on value investing at the Fordham University Graduate Business School starting in January 2016. Mr. Johnson is co-author of *The Gorilla Game, Picking Winners in High Technology*, was a contributing annotator in 2012 to *The Most Important Thing Illuminated*, by Howard Marks, and wrote the history of value investing in the forthcoming book celebrating the 100-year history of the Columbia Business School. Mr. Johnson is also co-author of the forthcoming, *Pitch the Perfect Investment, The Essential Guide to Winning on Wall Street*. Mr. Johnson has a B.A. in Economics from the University of California, Berkeley and an MBA in Finance from the Executive Program at the Wharton School of the University of Pennsylvania.

In January, 2003, the SEC commenced a civil enforcement action against Mr. Johnson, alleging two counts of securities fraud with respect to research reports on three companies prepared by Mr. Johnson, primarily from the failure to disclose personal financial interests in the companies that were the subject of the reports. On November 11, 2005, a jury returned a verdict finding that Mr. Johnson violated the federal securities laws in connection with the research reports. Mr. Johnson resolved the civil action and related administrative proceedings by entering into a settlement with the SEC (i) enjoining him, for a period of five (5) years, from future securities violations, (ii) requiring disgorgement of certain profits, (iii) requiring payment of a civil penalty and (iv) consenting to a five-year bar from association with any broker or dealer that ended on July 23, 2011.

We believe that Mr. Johnson brings to the Board extensive knowledge of corporate governance, corporate strategy, and capital allocation as well as shareholder value creation. This experience and knowledge led the Board to conclude that he should continue to serve as a director of the Company.

**THE BOARD OF DIRECTORS RECOMMENDS THAT YOU
VOTE FOR THE ELECTION OF THE ABOVE NOMINEES AS
DIRECTORS OF THE COMPANY.**

Directors Not Being Elected in 2015:

The directors whose terms are not expiring this year are listed below. They will continue to serve as directors for the remainder of their terms or until their respective successors are elected and qualified, or until their earlier death, resignation or removal. Information regarding each of such directors is provided below.

Class I Director With a Term That Will Expire at the 2016 Annual Meeting of Stockholders:

Name	Age	Position
Morton Taubman	72	Director, Chairman of the Audit Committee

Morton S. Taubman has served as a director since his appointment on March 10, 2006 to serve out the remaining term of G.W. Norman Wareham, who resigned his position on March 7, 2006. Mr. Taubman is also the Chairman of the Audit Committee and is a member of the Compensation Committee and the Corporate Governance and Nominating Committee. Mr. Taubman has experience as a certified public accountant and is currently an attorney with expertise in corporate law, government contracting and international relations. Prior to forming Hunter Taubman Fischer law firm, Mr. Taubman was the senior vice president and general counsel to DIGICON Corporation, an IT and telecommunications company. Before joining DIGICON, he was a senior partner at Ginsburg, Feldman and Bress, LLP, an established Washington, D.C. firm that provided expertise in tax, telecommunications, litigation, federal regulatory issues, capital reformation, government contracting and international issues. Before that, he was a founding partner at a number of law firms, was the partner-in-charge of the Washington D.C. office of Laventhol & Harworth, in charge of the Washington, D.C. tax department at Coopers & Lybrand and a special agent with the U.S. Treasury Department. Mr. Taubman has been an adjunct law professor for more than 15 years at Georgetown University and George Washington University. He presently also serves as special corporate counsel to Interior Systems, Inc. d/b/a ISI Professional Services, a United States federal contractor. He holds a Bachelor of Science Degree in Accounting from the University of Baltimore, a Juris Doctor Degree from the University of Baltimore Law School, and a Masters of Law Degree from Georgetown University.

Mr. Taubman brings to the Board financial expertise and is qualified as an audit committee financial expert. Mr. Taubman also brings to the Board a wealth of experience as a financial and legal professional serving as a partner at both major auditing and legal firms. This experience, as well as his independence from the Company and his prior performance as a Board member, led the Board to conclude that he should serve as a director of the Company.

Class II Directors With a Term That Will Expire at the 2017 Annual Meeting of Stockholders:

Name	Age	Position
Steve L. Komar	74	Chief Executive Officer, Director, and Chairman of the Board
James McCubbin	51	Executive Vice President, Chief Financial Officer, Secretary, Treasurer and Director

Steve L. Komar has served as a director since December 1997 and became Chairman of the Board in October 2001. Mr. Komar has also served as Chief Executive Officer since December 2001. From June 2000 until December 2001, Mr. Komar served as a founding partner of C-III Holdings, a development stage financial services company. From 1991 to June 2000, Mr. Komar served as Group Executive Vice President of Fiserv, Inc., a company that provides advanced data processing services and related products to the financial industry. From 1980 to 1991, Mr. Komar served in a number of financial management positions with CitiGroup, including the role of Chief Financial Officer of Diners Club International and Citicorp Information Resources, respectively. Mr. Komar is a graduate of the City University of New York with a Bachelor of Science Degree in Accounting and holds a Master's Degree in Finance from Pace University.

Mr. Komar brings extensive financial and operational management experience to the Board as a result of his past operational experience at several large firms where he held senior executive positions in areas including financial and operational management and mergers and acquisitions. The financial and managerial skills he developed over a career that has spanned more than 45 years, as well as Mr. Komar's experience as our Chairman of the Board and Chief Executive Officer, his knowledge of our Company as a result thereof, and his prior performance serving as a Board member of the Company, led the Board to conclude that he should continue to serve as a director of the Company.

James T. McCubbin has served as a director and as our Secretary since November 1998. Since August 1998, Mr. McCubbin has also served as our Executive Vice President and Chief Financial Officer. Prior to that time, from December 1997 to August 1998, Mr. McCubbin served as Vice President, Controller, Assistant Secretary and Treasurer. Prior to the commencement of his employment with WidePoint in November 1997, Mr. McCubbin held various financial management positions with several companies in the financial and government sectors. Mr. McCubbin is a graduate of the University of Maryland with a Bachelor of Science Degree in Finance and a Master's Degree in International Management. Mr. McCubbin brings extensive financial and corporate compliance expertise as well as internal knowledge of the Company as a result of his having over 13 years of experience with the Company. Mr. McCubbin also has significant experience serving in financial managerial roles within a variety of organizations and membership on several boards of directors over the past 25 years.

Mr. McCubbin also presently serves on the Board of Directors of ProPhase Labs, Inc. and serves on their Audit Committee. Mr. McCubbin was also on the Board of Directors of Redmile Entertainment until his resignation on March 1, 2008 and on the Board of Directors of Tianjin Pharmaceutical Company and was its Chairman of its Audit Committee, Nominating Committee, and Compensation Committee until his resignation on June 4, 2012. Mr. McCubbin subsequent to his resignation on the Board of Directors of Tianjin Pharmaceutical Company continued to serve as a consultant with the Company. Mr. McCubbin at times consultants on financial and other compliance matters. These experiences and his prior performance as a Board member led the Board to conclude that he should continue to serve as a director of the Company.

Board Meetings – Committees of the Board

The Board of Directors held 4 meetings during 2014. During this period, all of the directors attended or participated in more than 75% of the aggregate of the total number of meetings of the Board of Directors and the total number of meetings held by all Committees of the Board of Directors on which each such director served.

The Board currently has the following Committees: Audit; Corporate Governance and Nominating; and Compensation. Each Committee consists entirely of independent, non-employee directors in accordance with the listing standards of the NYSE MKT. Membership and principal responsibilities of the Board's Committees are described below. Each Committee of the Board has adopted a charter and each such charter is available free of charge on our website, www.widepoint.com, or by writing to WidePoint Corporation, 7926 Jones Branch Drive, Suite 520, McLean, Virginia 22102, c/o Corporate Secretary.

Audit Committee

The members of the Audit Committee are:

Morton S. Taubman (Chair)
James M. Ritter
George W. Norwood
Otto J. Guenther

The Audit Committee met four times in 2014. The Audit Committee has been established in accordance with Section 3(a)(58)(A) of the Securities and Exchange Act of 1934. The primary functions of the Audit Committee are to: appoint (subject to stockholder approval), and be directly responsible for the compensation, retention and oversight of, the firm that will serve as the Company's independent accountants to audit our financial statements and to perform services related to the audit (including the resolution of disagreements between management and the independent accountants regarding financial reporting); review the scope and results of the audit with the independent accountants; review with management and the independent accountants, prior to the filing thereof, the annual and interim financial results (including Management's Discussion and Analysis) to be included in our Forms 10-K and 10-Q, respectively; consider the adequacy and effectiveness of our internal accounting controls and auditing procedures; review, approve and thereby establish procedures for the receipt, retention and treatment of complaints received by the Company regarding accounting, internal accounting controls or auditing matters and for the confidential, anonymous submission by employees of concerns regarding questionable accounting or auditing matters; review and approve related person transactions in accordance with the policies and procedures of the Company; and consider the accountants' independence and establish policies and procedures for pre-approval of all audit and non-audit services provided to

WidePoint by the independent accountants who audit its financial statements. At each meeting, Audit Committee members may meet privately with representatives of Moss Adams LLP, our independent accountants, and with the Company's Executive Vice President and Chief Financial Officer.

The Board has determined that Messrs. Taubman, Ritter, Norwood and Guenther each meet the definition of "independent directors" for purposes of serving on an audit committee under applicable rules of the Securities and Exchange Commission and the listing standards of the NYSE MKT. In addition, the Board has determined that Mr. Taubman satisfies the "financially sophisticated" requirements set forth in the NYSE MKT Company Guide, and has designated Mr. Taubman as the "audit committee financial expert," as such term is defined in the rules and regulations of the SEC.

Corporate Governance and Nominating Committee

The members of the Corporate Governance and Nominating Committee are:

.	James M. Ritter (Chair)
.	Morton S. Taubman
.	Otto J. Guenther
.	George W. Norwood

The Corporate Governance and Nominating Committee met 1 time in 2014. The primary functions of this Committee are to: identify individuals qualified to become Board members and recommend to the Board the nominees for election to the Board at the next Annual Meeting of Stockholders; review annually and recommend changes to the Company's Corporate Governance Guidelines; lead the Board in its annual review of the performance of the Board and its committees; review policies and make recommendations to the Board concerning the size and composition of the Board, the qualifications and criteria for election to the Board, retirement from the Board, compensation and benefits of non-employee directors, the conduct of business between WidePoint and any person or entity affiliated with a director, and the structure and composition of the Board's Committees; review the Company's policies and programs relating to compliance with its Code of Business Conduct and such other matters as may be brought to the attention of the Committee regarding WidePoint's role as a responsible corporate citizen. See "Identification and Evaluation of Director Candidates" and "Director Compensation" in this proxy statement.

Compensation Committee

The members of the Compensation Committee are:

.	James M. Ritter (Chair)
.	Morton S. Taubman

.
.

George W. Norwood
Otto J. Guenther

The Compensation Committee met 2 times in 2014. The primary functions of the Compensation Committee are to: evaluate and approve executive compensation plans, policies and programs, including review of relevant corporate and individual goals and objectives, as submitted by the Chief Executive Officer; evaluate the Chief Executive Officer's performance relative to established goals and objectives and, together with the other independent directors, determine and approve the Chief Executive Officer's compensation level based on this evaluation; review and approve the annual salary and other remuneration of all other officers; review the management development program, including executive succession plans; review with management, prior to the filing thereof, the executive compensation disclosure included in this proxy statement; recommend individuals for election as officers; and review or take such other action as may be required in connection with the bonus, stock and other benefit plans of WidePoint and its subsidiaries.

Director Independence

The listing standards of the NYSE MKT require that our Board be comprised of a majority of "independent directors" and that the Audit Committee, Compensation Committee and Corporate Governance and Nominating Committee each be comprised solely of "independent directors," as defined under the listing standards of the NYSE MKT.

The Company's Corporate Governance and Nominating Committee conducts an annual review of the independence of the members of the Board and its Committees and reports its findings to the full Board of Directors. Based on the report and recommendation of the Corporate Governance Committee, the Board has determined that each of the Company's non-employee directors and its director nominee—Messrs. Taubman, Ritter, Guenther, Norwood and Johnson—satisfy the independence criteria (including the enhanced criteria with respect to members of the Audit Committee) set forth in the listing standards of the NYSE MKT and Securities and Exchange Commission rules. Each of the Board's Committees consists entirely of independent, non-employee directors.

Identification and Evaluation of Director Candidates

The Corporate Governance and Nominating Committee is charged with seeking individuals qualified to become directors and recommending candidates for all directorships to the full Board of Directors. The Committee considers director candidates in anticipation of upcoming director elections and other potential or expected Board vacancies.

The Committee considers director candidates suggested by members of the Committee, other directors, senior management and stockholders.

Director candidates are reviewed by the Committee based on the needs of the Board and the Company's various constituencies, their relative skills, characteristics and age, and against the following qualities and skills that are considered desirable for Board membership: exemplification of the highest standards of personal and professional integrity; independence from management under applicable securities laws, listing standards, and the Company's Corporate Governance Principles; experience and industry and educational background; potential contribution to the composition, diversity and culture of the Board; and ability and willingness to constructively challenge management through active participation in Board and committee meetings and to otherwise devote sufficient time to Board duties.

The Committee's charter includes diversity as one of the criteria used to evaluate director candidates. The Corporate Governance and Nominating Committee may consider diversity in its broadest sense when evaluating candidates. Though we do not have a formal policy regarding how diversity will be considered in identifying potential director nominees, our Corporate Governance Guidelines direct that the evaluation of nominees should include (but not be limited to) an assessment of whether a nominee would provide the Board with a diversity of viewpoints, backgrounds, experiences, and other demographics.

In evaluating the needs of the Board, the Committee considers the qualifications of sitting directors and consults with other members of the Board, the Chief Executive Officer and other members of senior management. All recommended candidates must possess the requisite personal and professional integrity, meet any required independence standards, and be willing and able to constructively participate in, and contribute to, Board and committee meetings. Additionally, the Committee conducts regular reviews of current directors whose terms are nearing expiration, but who may be proposed for re-election, in light of the considerations described above and their past contributions to the Board.

The Corporate Governance and Nominating Committee has adopted a policy pursuant to which a stockholder who has owned at least 5% of the Company's outstanding shares of common stock for at least two years may recommend a director candidate that the Committee will consider when there is a vacancy on the Board either as a result of a director resignation or an increase in the size of the Board. Such recommendation must be made in writing addressed to the Chairman of the Corporate Governance and Nominating Committee at the Company's principal executive offices and must be received by the Chairman at least 120 days prior to the anniversary date of the release of the prior year's proxy statement.

Although the Committee has not formulated any specific minimum qualifications that the Committee believes must be met by a nominee that the Committee recommends to the Board, the factors it will take into account will include strength of character, mature judgment, career specialization, relevant technical skills or financial acumen, diversity of viewpoint and industry knowledge. There will be no differences between the manner in which the Committee evaluates a nominee recommended by a stockholder and the manner in which the Committee evaluates nominees recommended by other persons.

The Company did not receive in a timely manner, in accordance with the Securities and Exchange Commission's requirements, any recommendation of a director candidate from a stockholder, or group of stockholders, that beneficially owned more than 5% of the Company's common stock for at least two years as of the date of recommendation.

Process for Communicating with Board Members

Interested parties may communicate directly with the Board, or the presiding director for an upcoming meeting or the non-employee directors as a group, by writing to WidePoint Corporation, 7926 Jones Branch, Suite 520, McLean, Virginia 22102, c/o Corporate Secretary. Communications may also be sent to individual directors at the above address.

Director Attendance at Annual Meetings

The Company has adopted a policy that each director should attempt to attend and/or be available via online access or phone for each Annual Meeting of Stockholders. All members of the Board were available and/or attended last year's Annual Meeting of Stockholders.

Board Leadership Structure and Role in Risk Oversight

Our Corporate Governance Guidelines allow flexibility as to whether the role of Chief Executive Officer and Chairman of the Board are separated or combined. The Board's policy is to adopt the practice that best serves the Company at any point in time. At this time, the Board believes that combining the role of Chairman of the Board with the role of Chief Executive Officer provides the most effective and efficient leadership model for the Company. Combining the Chairman and Chief Executive Officer roles fosters clear accountability, effective decision-making and alignment on corporate strategy. Currently, Steve L. Komar serves as our Chief Executive Officer and as our Chairman of the Board.

Because we have combined the Chairman and Chief Executive Officer roles, pursuant to our Corporate Governance Guidelines, our independent directors have designated Mr. Ritter to serve as the Presiding Independent Director to further strengthen our governance structure. The Presiding Independent Director is responsible for coordinating the activities of the independent directors, calling for meetings or sessions of the independent directors, presiding at executive sessions and coordinating the agenda for such sessions with at least two such meetings being held annually,

facilitating communications and functioning as principal liaison on Board-wide issues between independent directors and the Chairman of the Board, and when necessary, recommending the retention of outside advisors and consultants who report directly to Board.

Non-management members of the Board of Directors conduct at least two regularly scheduled meetings per year without members of management being present. Following an executive session of non-employee directors, the Presiding Independent Director may act as a liaison between the non-employee directors and the Chairman, provide the Chairman with input regarding agenda items for Board of Directors and Committee meetings, and coordinate with the Chairman regarding information to be provided to the non-employee directors in performing their duties.

The Board oversees the management of the risks inherent in the operation of the Company's business. This is accomplished principally through the Audit Committee. Additionally, the Compensation Committee is responsible for overseeing the assessment of risks associated with the Company's compensation policies and programs. Each of these committees receives and discusses reports regularly with members of management who are responsible for applicable day-to-day risk management functions of the Company, and reports regularly to the Board. The Board's, the Audit Committee's and the Compensation Committee's respective roles in our risk oversight process have not affected our Board leadership structure.

Director Compensation

Directors who are not also officers or employees receive an annual fee of \$12,000; however, for a six month period in fiscal 2014, each director voluntarily agreed to a 10% reduction in director fees beginning on June 1, 2014 and ending on December 31, 2014. The following table sets forth director compensation for the year ended December 31, 2014:

Director Name	Fees Earned or Paid (\$)	Option Awards (\$)	All Other Compensation (\$)	Total
James Ritter	\$ 11,400	\$ -	\$ -	\$ 11,400
Morton Taubman	\$ 11,400	\$ -	\$ -	\$ 11,400
George Norwood	\$ 11,400	\$ -	\$ -	\$ 11,400
Otto Guenther	\$ 11,400	\$ -	\$ -	\$ 11,400

Section 16(A) Beneficial Ownership Reporting Compliance

Section 16(a) of the Securities Exchange Act of 1934, as amended, requires the Company's officers and directors, and persons who own more than 10% of a registered class of the Company's equity securities, to file reports of securities ownership and changes in such ownership with the Securities and Exchange Commission. Statements of Changes in Beneficial Ownership of Securities on Form 4 are generally required to be filed before the end of the second business day following the day on which the change in beneficial ownership occurred. Based on the Company's review of

Forms 3 and 4 filed during 2014, all such Forms 3 and Forms 4 were filed on a timely basis.

Executive Officers

The Company's executive officers are as follows:

Name	Age	Position
Steve L. Komar	74	Chief Executive Officer, Director, and Chairman of the Board
James McCubbin	51	Executive Vice President, Chief Financial Officer, Secretary, Treasurer and Director
Jin Kang	51	Executive Vice President, Chief Operations Officer, Chief Executive Officer and President of iSYS LLC

For information with respect to Steve L. Komar and James McCubbin, please see the information about the members of our Board of Directors on the preceding pages. There are no family relationships among any of our executive officers or directors.

Jin Kang has served as Executive Vice President and Chief Operations Officer of WidePoint since June 30, 2012. Mr. Kang was appointed Chief Operations Officer on June 30, 2012. Mr. Kang has also served as the Chief Executive Officer and President of iSYS, a wholly-owned subsidiary of the Company, since our acquisition of iSYS on January 4, 2008. Mr. Kang founded the company in 1999 and has managed iSYS since its inception. Mr. Kang has over 26 years of professional experience in the Federal Government Information Technology Services field. Prior to founding iSYS, Mr. Kang was a Division Manager for Science Applications International Corporation (SAIC). His responsibilities included the Combined DNA Index System (CODIS), a marquee program for the FBI Laboratory Division. As the Engineering Manager for Northrop Grumman Corporation, Mr. Kang played a critical role in the successful management of the Defense Medical Information Systems/Systems Integration, Design Development, Operations and Maintenance Services (D/SIDDOMS) contract from its inception with zero revenues to a program of \$190 million in sales. Mr. Kang received a Bachelor and Master's Degrees in Computer Science and Computer Systems Management from the University of Maryland.

Principal Stockholders

Security Ownership of Directors and Executive Officers

The following tables set forth the number of shares of our common stock beneficially owned as of October 23, 2015 by each director, director nominee, executive officer and beneficial owner of more than 5% of the outstanding shares of the common stock as of October 23, 2015. In general, “beneficial ownership” includes those shares a director or executive officer has the power to vote or transfer, except as otherwise noted, and shares underlying warrants and stock options that are exercisable currently or within 60 days. The calculation of the percentage of outstanding shares is based on 82,520,696 shares outstanding as of October 23, 2015. The mailing address for each of our directors, director nominees and officers is 7926 Jones Branch Drive, Suite 520, McLean, Virginia 22102.

Directors, Nominees and Executive Officers	Number of Shares of Common Stock (1)	Percent of Common Stock Outstanding (1)	
Steve Komar (2)	2,112,803	2.6	%
Morton Taubman (3)	62,000	*	
James McCubbin (4)	1,875,203	2.3	%
James Ritter (5)	90,500	*	
Jin Kang (6)	2,993,677	3.6	%
Otto Guenther (7)	62,000	*	
George Norwood (8)	62,000	*	
Paul Johnson (9)	50,000	*	
All directors, director nominees and officers as a group (8 persons) (10)	7,308,183	8.9	%

5% Beneficial Owners	Number of Shares of Common Stock (1)	Percent of Common Stock Outstanding (1)	
Nokomis Capital, L.L.C. (11)	12,774,251	15.5	%

* Less than 1%.

(1) Assumes in the case of each stockholder listed above that all warrants or options held by such stockholder that are exercisable currently or within 60 days of October 23, 2013 were fully exercised by such stockholder, without the

exercise of any warrants or options held by any other stockholders.

Includes (i) 1,319,700 shares owned directly by Mr. Komar (excludes 250,000 shares of unvested restricted stock (2) awards not vesting within 60 days), and (ii) 793,103 shares held by SLK Diversified L.P., a limited partnership controlled by Mr. Komar, as a result of which such shares are held by Mr. Komar indirectly.

(3) Includes 62,000 shares subject to exercisable options to purchase shares of Common Stock, consisting of (i) 12,000 shares that may be purchased at a price of \$2.70 per share through March 10, 2016, pursuant to a director stock option granted on March 10, 2006 and (ii) 50,000 shares that may be purchased at a price of \$0.54 per share through May 11, 2019, pursuant to a stock option granted on May 11, 2009.

(4) Excludes 250,000 shares of unvested restricted stock awards not vesting within 60 days.

(5) Includes (i) 65,500 shares owned directly by Mr. Ritter and (ii) 25,000 shares of Common Stock that may be purchased at a price of \$0.54 per share through May 11, 2019, under an option granted on May 11, 2009.

(6) Includes (i) 2,880,344 shares owned directly by Mr. Kang, and (ii) 113,333 shares subject to exercisable options to purchase shares from the Company. Excludes from shares owned 81,667 unvested options to purchase shares of common stock.

(7) Includes 62,000 shares subject to exercisable options to purchase shares Common Stock, consisting of (i) 12,000 shares that may be purchased at a price of \$0.93 per share through August 15, 2017, pursuant to a director stock option granted on August 15, 2007 and (ii) 50,000 shares that may be purchased at a price of \$0.54 per share through May 11, 2019, pursuant to a stock option granted on May 11, 2009.

(8) Includes 62,000 shares subject to exercisable options to purchase shares Common Stock, consisting of (i) 12,000 shares that may be purchased at a price of \$0.93 per share through August 15, 2017, pursuant to a director stock option granted on August 15, 2007 and (ii) 50,000 shares that may be purchased at a price of \$0.54 per share through May 11, 2019, pursuant to a stock option granted on May 11, 2009.

(9) Includes 50,000 shares subject to exercisable options to purchase shares of Common Stock that may be purchased at a price of \$1.60 per share through February 11, 2016.

(10) Includes the shares referred to as included in notes (2) through (9) above.

(11) Information derived from Amendment No. 1 to Schedule 13G filed on October 2, 2015 and a Form 4 filed on September 22, 2015 on behalf of Nokomis Capital, L.L.C., a Texas limited liability company (“Nokomis Capital”), and Mr. Brett Hendrickson, the principal of Nokomis Capital. Nokomis Capital serves as the investment adviser to certain private funds and managed accounts (collectively, the “Nokomis Accounts”) and may direct the vote and dispose of the shares of common stock held by the Nokomis Accounts. As the principal of Nokomis Capital, Mr. Hendrickson may direct the vote and disposition of the shares of common stock held by the Nokomis Accounts. Pursuant to Rule 16a-1, both Nokomis Capital and Mr. Hendrickson disclaim such beneficial ownership. The principal office of Nakomis Capital is located at 2305 Cedar Springs Rd., Suite 420, Dallas, TX 75201.

Executive Compensation

Compensation Discussion and Analysis

This compensation discussion and analysis describes the material elements of compensation awarded to, earned by, or paid to each of our named executive officers, whom we refer to as our “NEOs,” during 2014 and describes our policies and decisions made with respect to the information contained in the following tables, related footnotes and narrative for 2014. The NEOs are identified below in the table titled “Summary Compensation Table.” In this compensation discussion and analysis, we also describe various actions regarding NEO compensation take before or after 2014 when we believe it enhances the understanding of our executive compensation program.

Overview of Our Executive Compensation Philosophy and Design

We believe that a skilled, experienced and dedicated executive and senior management team is essential to the future performance of our Company and to building stockholder value. We have sought to establish competitive compensation programs that enable us to attract and retain executive officers with these qualities. The other objectives of our compensation programs for our executive officers are the following:

- to motivate our executive officers to achieve strong financial performance;

- to attract and retain executive officers who we believe have the experience, temperament, talents and convictions to contribute significantly to our future success; and

- to align the economic interests of our executive officers with the interests of our stockholders.

Setting Executive Compensation

Our compensation committee has primary responsibility for, among other things, determining our compensation philosophy, evaluating the performance of our NEOs, setting the compensation and other benefits of our NEOs, overseeing the Company’s response to the outcome of the advisory votes of stockholders on executive compensation, assessing the relative enterprise risk of our compensation program and administering our equity compensation plans. The Company’s compensation planning is done annually for cash based performance goals and in multi-year periods

for equity based performance goal setting.

It is our Chief Executive Officer's responsibility to provide recommendations to the Compensation Committee for most compensation matters related to executive compensation. The recommendations are based on a general analysis of market standards and trends and an evaluation of the contribution of each executive officer to the Company's performance. Our Compensation Committee considers, but retains the right to accept, reject or modify such recommendations and has the right to obtain independent compensation advice. Neither the Chief Executive Officer nor any other members of management is present during executive sessions of the Compensation Committee. The Chief Executive Officer is not present when decisions with respect to his compensation are made. Our Board of Directors appoints the members of our compensation committee and delegates to the compensation committee the direct responsibility for overseeing the design and administration of our executive compensation program.

We have not historically utilized a compensation consultant to set the compensation of our NEOs.

Elements of Executive Compensation

We believe the most effective compensation package for our NEOs is one designed to reward achievement of individual and corporate objectives, provide for short-term, medium-term and long-term financial and strategic goals and align the interest of management with those of the stockholders by providing incentives for improving stockholder value. Compensation for our NEOs consists of base salary and an annual bonus opportunity, along with multi-year accelerated vesting goals associated with either stock option awards and or stock grant awards. Our annual bonus opportunity is intended to incentivize the achievement of goals that drive annual and multi-year performance, while our accelerated stock option and or stock grant vesting goals are intended to incentivize the achievement of goals that drive multi-year performance.

Base Salary. We pay our NEOs a base salary to compensate them for services rendered and to provide them with a steady source of income for living expenses throughout the year. The fiscal 2015 base salaries for our NEOs, as well as the percentage increase from the fiscal 2014 base salaries, are as follows:

Name	Fiscal 2015 Base Salary	Percentage Increase	
		Over Fiscal 2014 Base Salary	
Steve Komar	\$ 270,000	8	%(1)
James McCubbin	\$ 265,000	6	%(1)
Jin Kang	\$ 265,000	11	%(1)

(1) NEOs original base salary for fiscal 2014 included a voluntarily agreed to 10% reduction in base salary for five months. This voluntary reduction ended on December 31, 2014. In addition, the fiscal 2015 base salaries were increased on April 9, 2015.

Annual Cash Based Bonus Opportunity. The amount of the annual discretionary cash based bonus award is based on individual performance assessments along with the financial performance of the Company. Our performance-based cash incentive compensation in recent years has included targets for achieving various levels of revenue, operating income, and other financial goals and metrics, along with individual performance assessments that has included goals in personal professional improvement, team building, and other individual personal growth goals. The annual cash based bonus opportunity is for up to 50% of a NEOs base salary. In 2014, none of our NEOs earned a bonus because due to our net operating losses.

We believe these cash based award opportunities reinforce the alignment of interests of our executive officers with those of our stockholders in the shorter term as the positive financial performance that drives the cash based bonus awards also indirectly influences the performance of the Company's common stock. We believe the personal professional improvement goals enhance the value of the NEO to expand their expertise and expand the effectiveness of the Company's staff allowing for greater organization efficiencies while improving Company performance, which drives short-term, medium-term, and long-term organizational improvement and ultimately value for the stockholders in the form of better financial and common stock performance.

Restricted Stock Equity Awards. Mr. Komar and Mr. McCubbin were each awarded 250,000 shares of restricted common stock in 2010 that vest 100% upon the earlier of (i) the seventh anniversary from the date of grant or (ii) upon an acceleration event that is determined by the Compensation Committee.

Stock Option Equity Awards. Mr. Kang was awarded 170,000 stock options in 2013 that vest one third per year over a term of three years in order to reward Mr. Kang for improved performance in the Company's common stock price. On May 8, 2015, Mr. Kang was awarded 25,000 stock options that vest 50% on each of December 31, 2015 and 2016.

Acceleration of Equity Awards. The acceleration of the common shares and or stock options are tied generally to performance measures such as earnings before interest, taxes, amortization and depreciation and other triggers predominately tied to performance goals of the Company. In keeping with our philosophy for incentivizing the performance of our named executive officers over a medium to longer term horizon the Company has used equity grants and awards linked to accelerated vesting goals to reinforce the alignment of interest of our named executive officers with those of our stockholders, as the value of the awards granted thereunder is linked to the value of our Common Stock, which, in turn, is indirectly attributable to the performance of our executive officers.

Retirement and Other Benefits. We are strongly committed to encouraging all employees to save for retirement. To provide employees with the opportunity to save for retirement on a tax-deferred basis, we sponsor a defined contribution 401(k) savings plan. We also provide health, dental, vision and short term disability insurance to our NEOs on the same basis offered to all of our employees.

Summary Compensation Table

The following table summarizes the compensation paid by us in each of the last three recently completed fiscal years for our NEOs:

Name and Principal Position	Year	Base Salary (1)	Discretionary Bonus	Equity Awards (2)	Other Compensation (3)	Total Compensation
Steve Komar Chief Executive Officer, Director, and Chairman of the Board	2014	\$ 249,167 (4)	\$ -	\$ -	\$ 7,200	\$ 256,367
	2013	\$ 255,000	\$ -	\$ -	\$ 7,200	\$ 262,200
	2012	\$ 230,000	\$ -	\$ -	\$ 7,200	\$ 237,200
James McCubbin Executive Vice President, Chief Financial Officer, Secretary, Treasurer and Director	2014	\$ 249,167 (4)	\$ -	\$ -	\$ 7,200	\$ 256,367
	2013	\$ 255,000	\$ -	\$ -	\$ 7,200	\$ 262,200
	2012	\$ 230,000	\$ -	\$ -	\$ 7,200	\$ 237,200
Jin Kang Executive Vice President & Chief Operations Officer	2014	\$ 239,583 (4)	\$ -	\$ -	\$ -	\$ 239,583
	2013	\$ 250,000	\$ -	\$ 96,900 (5)	\$ -	\$ 346,900
	2012	\$ 250,000	\$ 20,000	\$ -	\$ -	\$ 270,000

(1) Amount represents base salary as set forth in an executive employment agreement.

(2) Amount represents the grant date fair value calculated pursuant to ASC Topic 718. Additional information about the assumptions used when valuing equity awards is set forth in the notes the consolidated financial statements included in the Company's Form 10-K for the year ended December 31, 2014.

(3) Monthly combined home office and phone allowance of \$600 were paid to Mr. Komar and Mr. McCubbin during fiscal 2014, 2013 and 2012.

(4) For a five month period in fiscal year 2014, Mr. Komar, Mr. McCubbin and Mr. Kang each voluntarily agreed to a 10% reduction in base salary.

(5) During fiscal 2013 Mr. Kang was granted an equity award of 170,000 options on March 21, 2013 with an estimated fair value of approximately \$96,900.

Grant of Plan Based Awards

None of our NEOs received equity awards in fiscal 2014.

Outstanding Equity Awards at December 31, 2014

The following table sets forth information on outstanding equity awards held by NEOs at December 31, 2014:

Name	Option Awards					Stock Awards	
	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Exercised Options (#) Unexercisable	Equity Incentive Plan Awards: Number of Securities Underlying Unearned Options (#)	Option Exercise Price (\$)	Option Expiration Date	Equity Incentive Plan Awards: Unearned Shares or other Rights that have not Vested (#)	Equity Incentive Plan Awards: Market or Payout Value of Unearned Shares or Rights that have not Vested (\$)
Steve L. Komar, Chief Executive Officer, Director, and Chairman of the Board	-	-	-	-	-	250,000(1)	\$ 345,000
James T. McCubbin, Executive Vice President, Chief Financial Officer, Secretary, Treasurer and Director	-	-	-	-	-	250,000(1)	\$ 345,000
Jin Kang, Executive Vice President, Chief Operations Officer, Chief Executive Officer and President of iSYS LLC	56,666	113,334	-	\$ 0.57	3/20/2018 (2)	-	-

(1) Equity incentive plan awards unearned represent restricted stock awards, which vest on the seventh anniversary of the date of grant or earlier upon a determination by the compensation committee that such shares have been earned.

(2) Options vest one-third per year over a term of three years.

Option Exercises and Stock Vested for Fiscal 2014

None of our NEOs exercised options or had stock vest during the year ended December 31, 2014.

Employment Agreements and Compensation Arrangements;

Termination and Change in Control Provisions

The following describes the terms of employment agreements between the Company and the named executive officers included in the above Summary Compensation Table and sets forth information regarding potential payments upon termination of employment or a change in control of the Company.

Mr. Komar. On April 9, 2015, we entered into an amendment of an employment agreement with Steve Komar, our Chief Executive Officer and President, dated as of August 13, 2010 and effective as of July 1, 2010. The employment agreement, as amended, has a term expiring on December 31, 2015. The agreement provides for (1) a base salary of \$270,000, (2) a home office/automobile expense allowance of \$600 per month to cover such expenses incurred in the pursuit of our business; (3) a phone allowance of \$100 per month to cover such expenses incurred in the pursuit of our business; (4) reimbursement for additional actual business expenses consistent with our existing policies that have been incurred for our benefit; (5) paid medical and other benefits consistent with our existing policies with respect to our key executives, as such policies may be amended from time to time in the future; and (6) performance incentive bonuses as may be granted annually at the discretion of the Compensation Committee of the Board. For a five month period in calendar 2014, Mr. Komar voluntarily agreed to a 10% reduction in base salary.

The employment agreement contains a severance provision which provides that upon the termination of his employment without Cause (as described below) or his voluntary resignation for a Good Reason (as described below), Mr. Komar will receive severance compensation payable in a lump-sum of cash equal to the greater of (a) an amount equal to twelve (12) months of his base salary then in effect, or (b) an amount equal to Mr. Komar's base salary for the remainder of the term of the employment agreement as if the employment agreement had not been terminated; provided that if employment terminates by reason of death or disability, then Mr. Komar shall receive a one-time payment equal to the amount of Base Salary owed for the immediate twelve (12) months following the death or disability event, or an amount equal the remainder of the contractual term of the employment agreement whichever is less and all granted but unvested stock options shall be immediately vested and the period of exercise extended for an additional 2 years.

The employment agreement further provides that if within two years after a change in control of the Company there occurs any termination of Mr. Komar for any reason other than for Cause or a voluntary resignation without a Good Reason, then the Company will be required to pay to Mr. Komar a one-time severance payment equal to the greater of (a) an amount equal to twelve (12) months of his base salary then in effect, or (b) an amount equal to Mr. Komar's base salary for the remainder of the term of the employment agreement. If Mr. Komar's employment terminates for any reason other than for Cause or a voluntary retirement without Good Reason, Mr. Komar will be eligible to participate, at the Company's expense, in all executive medical and dental plans provided by the Company for the remainder of the term of the employment agreement. Mr. Komar will receive a payment equal to any excise, income and other taxes resulting from the imposition of parachute penalties of the Internal Revenue Code or applicable state tax law.

Termination of Mr. Komar's employment by the Company shall be deemed for "Cause" if, and only if, it is based upon (i) conviction of a felony by a federal or state court of competent jurisdiction; (ii) material disloyalty to the Company such as embezzlement or misappropriation of corporate assets; or (iii) engaging in unethical or illegal behavior which is of a public nature, brings the Company into disrepute, and results in material damage to the Company. A resignation by Mr. Komar shall not be deemed to be voluntary and shall be deemed to be a resignation with "Good Reason" if it is based upon (i) a diminution in Mr. Komar's title, duties, or salary; (ii) a material reduction in benefits; (iii) a direction by the Board of Directors that Mr. Komar report to any person or group other than the Board of Directors, or (iv) a geographic relocation of the Company's primary business operations outside of the Washington Metropolitan Area.

Mr. McCubbin. On April 9, 2015, we entered into an amendment of an employment agreement with James T. McCubbin, our Executive Vice President, Chief Financial Officer, Secretary and Treasurer, dated as of August 13, 2010 and effective as of July 1, 2010. The amendment to Mr. McCubbin's employment agreement has a term expiring on March 31, 2017. The agreement provides for (1) a base salary of \$265,000, (2) a home office/automobile expense allowance of \$600 per month to cover such expenses incurred in the pursuit of our business; (3) a phone allowance of \$100 per month to cover such expenses incurred in the pursuit of our business; (4) reimbursement for additional actual business expenses consistent with our existing policies that have been incurred for our benefit; (5) paid medical and other benefits consistent with our existing policies with respect to our key executives, as such policies may be amended from time to time in the future; and (6) performance incentive bonuses as may be granted annually at the discretion of the Compensation Committee of the Board. For a five month period in calendar 2014, Mr. McCubbin voluntarily agreed to a 10% reduction in base salary.

The employment agreement contains a severance provision which provides that upon the termination of his employment without Cause (as described below) or his voluntary resignation for a Good Reason (as described below), Mr. McCubbin will receive severance compensation payable in a lump-sum of cash equal to the greater of (a) an amount equal to twelve (12) months of his base salary then in effect, or (b) an amount equal to Mr. McCubbin's base salary for the remainder of the term of the employment agreement as if the employment agreement had not been terminated; provided that if employment terminates by reason of death or disability, then Mr. McCubbin shall receive a one-time payment equal to the amount of Base Salary owed for the immediate twelve (12) months following the death or disability event, or an amount equal the remainder of the contractual term of the employment agreement whichever is less and all granted but unvested stock options shall be immediately vested and the period of exercise extended for an additional 2 years.

The employment agreement further provides that if within two years after a change in control of the Company there occurs any termination of Mr. McCubbin for any reason other than for Cause or a voluntary resignation without a Good Reason, then the Company will be required to pay to Mr. McCubbin a one-time severance payment equal to the greater of (a) an amount equal to twelve (12) months of his base salary then in effect, or (b) an amount equal to Mr. McCubbin's base salary for the remainder of the term of the employment agreement. If Mr. McCubbin's employment terminates for any reason other than for Cause or a voluntary retirement without Good Reason, Mr. McCubbin will be eligible to participate, at the Company's expense, in all executive medical and dental plans provided by the Company for the remainder of the term of the employment agreement. Mr. McCubbin will receive a payment equal to any excise, income and other taxes resulting from the imposition of parachute penalties of the Internal Revenue Code or applicable state tax law.

Termination of Mr. McCubbin's employment by the Company shall be deemed for "Cause" if, and only if, it is based upon (i) conviction of a felony by a federal or state court of competent jurisdiction; (ii) material disloyalty to the Company such as embezzlement or misappropriation of corporate assets; or (iii) engaging in unethical or illegal behavior which is of a public nature, brings the Company into disrepute, and results in material damage to the Company. A resignation by Mr. McCubbin shall not be deemed to be voluntary and shall be deemed to be a resignation with "Good Reason" if it is based upon (i) a diminution in Mr. McCubbin's title, duties, or salary; (ii) a material reduction in benefits; (iii) a direction by the Board of Directors that Mr. McCubbin report to any person or group other than the Board of Directors, or (iv) a geographic relocation of the Company's primary business operations outside of the Washington Metropolitan Area.

Mr. Kang. On April 9, 2015, we entered into an employment agreement with Jin Kang, our Executive Vice President and Chief Executive Officer of iSYS LLC and Chief Operations Officer, which replaced Mr. Kang's prior employment agreement, dated November 27, 2012. The agreement is for a term ending on December 31, 2016 and provides for (1) a base salary of \$265,000 per year, (2) reimbursement for business expenses, (3) medical and other benefits consistent with our existing policies with respect to our key executives, as such policies may be amended from time to time in the future, and (4) bonus compensation in the reasonable discretion of the Compensation Committee of the Board of Directors.

Mr. Kang's employment period will continue from the date of his agreement until December 31, 2016 unless he is terminated earlier due to (a) Mr. Kang's death or permanent disability which renders Mr. Kang unable to perform his duties hereunder (as determined by the Company in its good faith judgment), (b) Mr. Kang's resignation upon prior written notice to the Company of one-hundred and eighty (180) days, (c) termination by the Company for Cause or (d) termination by the Company without Cause upon prior written notice of one-hundred and eighty (180) days. "Cause" is defined in the Agreement as: (i) the repeated failure or refusal of Mr. Kang to follow the lawful directives of the Company, or its designee (except due to sickness, injury or disabilities), after prior notice to Mr. Kang and a reasonable opportunity to cure by Mr. Kang for up to thirty (30) days, (ii) gross inattention to duty or any other willful, reckless or grossly negligent act (or omission to act) by Mr. Kang, which, in the good faith judgment of the Company, materially injures the Company, including the repeated failure to follow the policies and procedures of the Company, after prior written notice to Employee and a reasonable opportunity to cure by Mr. Kang of up to thirty (30) days, (iii) a material breach of this Agreement by Mr. Kang, after prior written notice to Mr. Kang and a reasonable opportunity to cure by Mr. Kang of up to thirty (30) days, (iv) the commission by Mr. Kang of a felony or other crime involving moral turpitude or the commission by Mr. Kang of an act of financial dishonesty against the Company or, (v) a proper business purpose of the Company, which shall be limited to the elimination of the position filled by Mr. Kang as a result of a material decrease in revenues and/or profits of the Company, but with other cost cutting measures and the termination of other employees being first considered and instituted as determined in the sole judgment of the Company prior to the termination of Mr. Kang; provided, however, that in the event the Company terminates Mr. Kang under (v) above, then (I) the scope of the non-compete shall be limited to the products and services offered by the Company as of the termination of Mr. Kang and (II) the Company shall pay to Mr. Kang a continuation of base salary and benefits each month for the six (6) month period immediately following such termination. In the event Mr. Kang is terminated without Cause, then the Company shall pay to Mr. Kang a continuation of base salary and benefits each month for the six (6) month period immediately following such termination and the non-compete provisions in the agreement shall not apply.

Compensation Committee Interlocks and Insider Participation

During the last fiscal year, no member of the Compensation Committee had a relationship with us that required disclosure under Item 404 of Regulation S-K. During the past fiscal year, none of our executive officers served as a member of the board of directors or compensation committee, or other committee serving an equivalent function, of any entity that has one or more executive officers who served as members of our Board of Directors or our Compensation Committee. None of the members of our Compensation Committee is an officer or employee of our Company, nor have they ever been an officer or employee of our Company

Compensation Committee Report

Our Compensation Committee has reviewed and discussed the “Compensation Discussion and Analysis” contained herein with management. Based on our Compensation Committee’s review and discussions with management, our Compensation Committee recommended to our Board of Directors that the Compensation Discussion and Analysis be included herein.

James M. Ritter (Chair)

Morton S. Taubman

George W. Norwood

Otto J. Guenther

Certain Related Person Transactions

A related person transaction is a consummated or currently proposed transaction in which the Company has been, is or will be a participant and the amount involved exceeds \$120,000, and in which a related person (i.e., any director or executive officer or nominee for director, or any member of the immediate family of such person) has or will have a direct or indirect material interest.

The Company was not a participant in any related person transactions in the past two fiscal years and no such transactions are currently proposed.

Under the Company's corporate governance principles (the "Corporate Governance Principles"), a majority of the Company's Board will consist of independent directors. An "independent" director is a director who meets the NYSE MKT definition of independence and other applicable independence standards under SEC guidelines, as determined by the Board. The Company's Corporate Governance and Nominating Committee conduct an annual review of the independence of the members of the Board and its Committees and report its findings to the full Board of Directors. Based on the report and recommendation of the Corporate and Nominating Governance Committee, the Board has determined that each of the Company's non-employee directors—Messrs. Taubman, Ritter, Guenther, and Norwood—satisfies the independence criteria (including the enhanced criteria with respect to members of the Audit Committee) set forth in the applicable NYSE MKT listing standards and SEC rules. Each Board Committee consists entirely of independent, non-employee directors.

Non-management members of the Board of Directors conduct at least two regularly-scheduled meetings per year without members of management being present. Mr. Ritter serves as the presiding director of such meetings. Following an executive session of non-employee directors, the presiding director may act as a liaison between the non-employee directors and the Chairman, provide the Chairman with input regarding agenda items for Board of Directors and Committee meetings, and coordinate with the Chairman regarding information to be provided to the non-employee directors in performing their duties.

Proposal Two – Independent Accountants

The Audit Committee is recommending that stockholders ratify its appointment of Moss Adams LLP as independent accountants for WidePoint to audit its consolidated financial statements for the fiscal year ending December 31, 2015, to perform audit-related services, including review of our quarterly interim financial information, periodic reports and registration statements filed with the Securities and Exchange Commission and consultation in connection with various accounting and financial reporting matters. The stockholder vote is not binding on the Audit Committee. If the appointment of Moss Adams LLP is not ratified by stockholders, the Audit Committee will evaluate the basis for the stockholders' vote when determining whether to continue the firm's engagement, but may ultimately determine to continue the engagement of the firm or another audit firm without re-submitting the matter to stockholders. Even if the appointment of Moss Adams LLP is ratified, the Audit Committee may in its sole discretion terminate the engagement of the firm and direct the appointment of another independent auditor at any time during the year if it determines that such an appointment would be in the best interests of our Company and our stockholders.

Moss Adams LLP provided audit and other services in 2015 for the Company's audit of its consolidated financial statements for the fiscal year ended December 31, 2014. Moss Adams LLP also provided audit and other services in 2014 for the Company's audit of its consolidated financial statements for the fiscal year ended December 31, 2013.

A resolution will be presented at the Annual Meeting to ratify the appointment of Moss Adams LLP to serve as the Company's independent public accountants for the fiscal year ending December 31, 2015. A representative of Moss Adams LLP will be available either via phone or in person at the Annual Meeting to answer appropriate questions concerning the Company's financial statements and to make a statement if desired.

THE BOARD OF DIRECTORS RECOMMENDS THAT STOCKHOLDERS VOTE IN FAVOR OF THE RATIFICATION OF THE COMPANY'S AUDITORS.

Audit Committee Report

The Audit Committee has: (a) reviewed and discussed the audited financial statements with the management of the Company; (b) discussed with the Company's independent auditors, Moss Adams LLP, the matters required to be discussed by Statement on Auditing Standards No. 61; (c) received from the Company's independent auditors the written disclosures and the letter required by applicable requirements of the Public Company Accounting Oversight Board, and discussed with the Company's independent auditors their independence; and (d) based on the review and discussions referred to in clauses (a), (b) and (c) above, recommended to the Board that the audited financial statements be included in the Company's Annual Report on Form 10-K for fiscal year 2014.

The foregoing report is submitted by the members of the Audit Committee:

Morton S. Taubman (Chair)
James M. Ritter
George W. Norwood
Otto J. Guenther

Independent Registered Certified Public Accounting Firm Fees and Services

The following table sets forth fees paid to our principal accountants in connection with audit and audit-related, tax and other non-audit fees for the years ended December 31:

Service Type	2014	2013
Audit and Quarterly Review Fees(1)	\$174,864	\$185,456
Audit-Related Fees(2)	38,415	-
Tax Fees	-	-
All Other Fees	-	-
Total	\$213,279	\$185,456

(1) Audit and quarterly review fees for the annual audit and review of financial statements included in the Company's quarterly filings, including reimbursable expenses.

(2) Audit-Related fees for other required regulatory filings including Form S-3 consents included in the Company's filings, including reimbursable expenses.

Audit Committee Policies and Procedures For Pre-Approval of Independent Auditor Services

The following describes the Audit Committee's policies and procedures regarding pre-approval of the engagement of the Company's independent auditor to perform audit as well as permissible non-audit services for the Company.

For audit services, the independent auditor will provide the Audit Committee with an engagement letter during the March-May quarter of each year outlining the scope of the audit services proposed to be performed in connection with the audit of the current fiscal year. If agreed to by the Audit Committee, the engagement letter will be formally accepted by the Audit Committee at an Audit Committee meeting held as soon as practicable following receipt of the engagement letter. The independent auditor will submit to the Audit Committee for approval an audit services fee proposal after acceptance of the engagement letter.

For non-audit services, Company management may submit to the Audit Committee for approval (during May through September of each fiscal year) the list of non-audit services that it recommends the Audit Committee engage the independent auditor to provide for the fiscal year. The list of services must be detailed as to the particular service and may not call for broad categorical approvals. Company management and the independent auditor will each confirm to the Audit Committee that each non-audit service on the list is permissible under all applicable legal requirements. In addition to the list of planned non-audit services, a budget estimating non-audit service spending for the fiscal year may be provided. The Audit Committee will consider for approval both the list of permissible non-audit services and the budget for such services. The Audit Committee will be informed routinely as to the non-audit services actually provided by the independent auditor pursuant to this pre-approval process.

To ensure prompt handling of unexpected matters, the Audit Committee delegates to its Chairman the authority to amend or modify the list of approved permissible non-audit services and fees. The Chairman will report any action taken pursuant to this delegation to the Audit Committee at its next meeting.

All audit and non-audit services provided to the Company are required to be pre-approved by the Audit Committee. The Chief Financial Officer of the Company will be responsible for tracking all independent auditor fees against the budget for such services and report at least annually to the Audit Committee.

Other Information

We maintain an internet website at <http://www.widepoint.com>. Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and any amendment to those reports, are available free of charge on our website immediately after they are filed with or furnished to the Securities and Exchange Commission. WidePoint's Code of Business Conduct, Corporate Governance Principles and Charters of the Committees of the Board of Directors are also available free of charge on our website or by writing to WidePoint Corporation, 7926 Jones Branch Drive, Suite 520, McLean, Virginia 22102, c/o Corporate Secretary. WidePoint's Code of Business Conduct applies to all directors, officers (including the Chief Executive Officer and Chief Financial Officer) and employees. Amendments to or waivers of the Code of Conduct granted to any of the Company's directors or executive officers will be published on our website within five business days of such amendment or waiver.

Stockholder Proposals for 2016 Annual Meeting

Proposals of stockholders intended to be presented at the 2016 Annual Meeting must be received by the Secretary of the Company, 7926 Jones Branch, Suite 520, McLean, Virginia, no later than July 2, 2016 in order for them to be considered for inclusion in the 2016 Proxy Statement. Any such proposal must comply with Rule 14a-8 of Regulation 14A of the proxy rules of the Securities and Exchange Commission. A stockholder desiring to submit a proposal to be voted on at next year's Annual Meeting of Stockholders, but not desiring to have such proposal included in next year's proxy statement relating to that meeting, should submit such proposal to the Company no later than July 2, 2016. Failure to comply with that advance notice requirement will result in the proposal not being placed on the agenda at the meeting.

Other Matters

Management is not aware of any other matters to be considered at the Annual Meeting. If any other matters properly come before the Annual Meeting, the persons named in the enclosed Proxy will vote said Proxy in accordance with their discretion.

nbsp; We also expect to rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of such third parties could delay clinical development or marketing approval of our drug candidates or commercialization of our drugs, producing additional losses and depriving us of potential revenue from sales of drugs.

We intend to rely on third parties to conduct investigator-sponsored clinical trials of Selinexor and our other drug candidates. Any failure by a third party to meet its obligations with respect to the clinical development of our drug candidates may delay or impair our ability to obtain regulatory approval for Selinexor and our other drug candidates.

We intend to rely on academic and private non-academic institutions to conduct and sponsor clinical trials relating to Selinexor and our other drug candidates. We will not control the design or conduct of the investigator-sponsored trials, and it is possible that the FDA or non-U.S. regulatory authorities will not view these investigator-sponsored trials as providing adequate support for future clinical trials, whether controlled by us or third parties, for any one or more reasons, including elements of the design or execution of the trials or safety concerns or other trial results.

Such arrangements will provide us certain information rights with respect to the investigator-sponsored trials, including access to and the ability to use and reference the data, including for our own regulatory filings, resulting from the investigator-sponsored trials. However, we do not have control over the timing and reporting of the data from investigator-sponsored trials, nor do we own the data from the investigator-sponsored trials. If we are unable to confirm or replicate the results from the investigator-sponsored trials or if negative results are obtained, we would likely be further delayed or prevented from advancing further clinical development of our drug candidates. Further, if investigators or institutions breach their obligations with respect to the clinical development of our drug candidates, or if the data proves to be inadequate compared to the first-hand knowledge we might have gained had the investigator-sponsored trials been sponsored and conducted by us, then our ability to design and conduct any future clinical trials ourselves may be adversely affected.

Additionally, the FDA or non-U.S. regulatory authorities may disagree with the sufficiency of our right of reference to the preclinical, manufacturing or clinical data generated by these investigator-sponsored trials, or our interpretation of preclinical, manufacturing or clinical data from these investigator-sponsored trials. If so, the FDA or other non-U.S. regulatory authorities may require us to obtain and submit additional preclinical, manufacturing, or clinical data before we may initiate our planned trials and/or may not accept such additional data as adequate to initiate our planned trials.

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We contract with third parties for the manufacture of our drug candidates for preclinical studies and clinical trials and expect to continue to do so for clinical trials and ultimately for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our drug candidates or drugs or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not have any manufacturing facilities or personnel. We currently rely, and expect to continue to rely, on third-party manufacturers for the manufacture of our drug candidates for preclinical studies and clinical trials under the guidance of members of our organization. To date, we have obtained starting materials for our supply of the current good manufacturing practices, or cGMP, bulk drug substance for our drug candidates from one third-party manufacturer. We have engaged a separate third-party manufacturer for fill-and-finish services. We do not have a long term supply agreement with either of these third-party manufacturers, and we purchase our required drug supplies on a purchase order basis.

We expect to rely on third-party manufacturers or third-party collaborators for the manufacture of our drug candidates for clinical trials and ultimately for commercial supply of any of these drug candidates for which we or any of our future collaborators obtain marketing approval. We may be unable to establish any agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

reliance on the third party for regulatory compliance and quality assurance;

the possible breach of the manufacturing agreement by the third party;

the possible failure of the third party to manufacture our drug candidate according to our specifications;

the possible failure of the third party to manufacture our drug candidate according to our schedule, or at all;

the possible misappropriation by the third party or others of our proprietary information, including our trade secrets and know-how; and

the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside of the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of drug candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our drugs and harm our business and results of operations.

Any drugs that we may develop may compete with other drug candidates and drugs for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply or a second source for cGMP bulk drug substance or fill-and-finish services. If our current contract manufacturers cannot perform as agreed, we may be required to replace those manufacturers. Although we believe that there are several potential alternative manufacturers who could manufacture our drug candidates, we may incur added costs and delays in identifying and qualifying any such replacement.

Our current and anticipated future dependence upon others for the manufacture of our drug candidates or drugs may adversely affect our future profit margins and our ability to commercialize any drugs that receive marketing approval on a timely and competitive basis.

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Risks Related To Our Intellectual Property

If we are unable to obtain and maintain patent protection for our drug candidates and other discoveries, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize drugs and other discoveries similar or identical to ours, and our ability to successfully commercialize our drug candidates and other discoveries may be adversely affected.

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary drug candidates and other discoveries. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our novel drug candidates and other discoveries that are important to our business. To date, one patent has issued that relates to XPO1 inhibitors, other than our key drug candidates, and their use in targeted therapeutics. We cannot be certain that any patents will issue with claims that cover any of our key drug candidates or other discoveries or drug candidates.

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our drug candidates or other discoveries, or which effectively prevent others from commercializing competitive drugs and discoveries. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

The laws of foreign countries may not protect our rights to the same extent as the laws of the United States. For example, in some foreign jurisdictions, our ability to secure patents based on our filings in the United States may depend, in part, on our ability to timely obtain assignment of rights to the invention from the employees and consultants who invented the technology. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in our patent or pending patent applications, or that we were the first to file for patent protection of such inventions.

Assuming the other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside of the United States, the first to file a patent application is entitled to the patent. In March 2013, the United States transitioned to a first-inventor-to-file system in which, assuming the other requirements for patentability are met, the first inventor to file a patent application is entitled to the patent. We may be subject to a third-party preissuance submission of prior art to the U.S. Patent and Trademark Office, or become involved in opposition, derivation, revocation, reexamination, or post-grant or *inter partes* review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our discoveries or drugs and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize drugs without infringing third-party patent rights.

Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us

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with any competitive advantage. Our competitors may be able to circumvent our patents by developing similar or alternative discoveries or drugs in a non-infringing manner.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical discoveries and drugs, or limit the duration of the patent protection of our discoveries and drug candidates. Given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing drugs similar or identical to ours.

We may become involved in lawsuits to protect or enforce our patents and other intellectual property rights, which could be expensive, time-consuming and unsuccessful.

Competitors may infringe our patents and other intellectual property rights. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, or may refuse to stop the other party from using the intellectual property at issue. An adverse result in any litigation could put one or more of our patents at risk of being invalidated or interpreted narrowly. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability and the ability of any future collaborators that we may have to develop, manufacture, market and sell our drug candidates and use our proprietary technologies without infringing the proprietary rights of third parties. We may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our drug candidates and technology, including interference proceedings before the U.S. Patent and Trademark Office. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. No litigation asserting such infringement claims is currently pending against us, and we have not been found by a court of competent jurisdiction to have infringed a third party's intellectual property rights; however, if we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our drug candidates and using our technology. However, we may not be able to obtain any required license on commercially reasonable terms, or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same intellectual property licensed to us. We could be forced, including by court order, to cease commercializing the infringing intellectual property or drug or to cease using the infringing technology. In addition, we could be found liable for monetary damages. A finding of infringement could prevent us from commercializing our drug candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

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We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. Although we have no knowledge of any such claims being alleged to date, if such claims were to arise, litigation may be necessary to defend against any such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

Obtaining and maintaining our patent protection depends on compliance with various procedural, documentary, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to the United States Patent and Trademark Office, or USPTO, and various foreign patent offices at various points over the lifetime of the patents and/or applications. We have systems in place to remind us to pay these fees, and we rely on our outside counsel to pay these fees when due. Additionally, the USPTO and various foreign patent offices require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply with such provisions, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with rules applicable to the particular jurisdiction. However, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If such an event were to occur, it could have a material adverse effect on our business.

If we do not successfully extend the term of patents covering our drug candidates under the Hatch-Waxman Amendments and similar foreign legislation, our business may be materially harmed.

Depending upon the timing, duration and conditions of FDA marketing approval, if any, of our drug candidates, one or more of our U.S. patents may be eligible for patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman

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Amendments. The Hatch-Waxman Amendments permit a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. However, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request.

In the United States, only a single patent can be extended for each FDA approval, and any patent can be extended only once, for a single product. Laws governing analogous patent term extensions in foreign jurisdictions vary widely, as do laws governing the ability to obtain multiple patents from a single patent family. Because both Selinexor and Verdinexor are protected by a single family of patents and applications, we may not be able to secure patent term extensions for both of these drug candidates in all jurisdictions where these drug candidates are approved, if ever.

If we are unable to obtain a patent term extension for a drug candidate or the term of any such extension is less than we request, the period during which we can enforce our patent rights for that drug candidate, if any, in that jurisdiction will be shortened and our competitors may obtain approval to market competing products sooner. As a result, our revenue could be materially reduced.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for our drug candidates and other discoveries, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, outside scientific collaborators, contract research organizations, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. To the extent that we are unable to timely enter into confidentiality and invention or patent assignment agreements with our employees and consultants, our ability to protect our business through trade secrets and patents may be harmed. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside of the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

Our trademarks are not registered. Failure to secure those registrations could adversely affect our business.

Although we filed three intent to use applications with respect to our trademarks in the United States in August 2013, our trademarks are not yet registered in the United States or other countries. If we do not secure registrations for our trademarks, we may encounter more difficulty in enforcing them against third parties than we otherwise would, which could adversely affect our business. We have also not yet registered trademarks for any of our drug candidates in any jurisdiction. When we file trademark applications for our drug candidates those applications may not be allowed for registration, and registered trademarks may not be obtained, maintained or enforced. During trademark registration proceedings in the United States and foreign jurisdictions, we may receive rejections. We are given an opportunity to respond to those rejections, but we may not be able to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered

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trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings.

In addition, any proprietary name we propose to use with our key drug candidates in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed drug names, including an evaluation of potential for confusion with other drug names. If the FDA objects to any of our proposed proprietary drug names for any of our drug candidates, if approved, we may be required to expend significant additional resources in an effort to identify a suitable proprietary drug name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA.

Risks Related to Regulatory Approval and Other Legal Compliance Matters

Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the commercialization of some or all of our drug candidates. As a result, we cannot predict when or if we, or any collaborators we may have in the future, will obtain marketing approval to commercialize a drug candidate.

The research, testing, manufacturing, labeling, approval, selling, marketing, promotion and distribution of drugs are subject to extensive regulation by the FDA and comparable foreign regulatory authorities, whose laws and regulations may differ from country to country. We are not permitted to market our drug candidates in the United States or in other countries until we, or any collaborators we may have in the future, receive approval of an NDA from the FDA or marketing approval from applicable regulatory authorities outside of the United States. Our drug candidates are in early stages of development and are subject to the risks of failure inherent in drug development. We have not submitted an application for or received marketing approval for any of our drug candidates in the United States or in any other jurisdiction. We have limited experience in conducting and managing the clinical trials necessary to obtain marketing approvals, including FDA approval of an NDA.

The process of obtaining marketing approvals, both in the United States and abroad, is a lengthy, expensive and uncertain process. It may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the drug candidates involved.

In addition, changes in marketing approval policies during the development period, changes in or the enactment or promulgation of additional statutes, regulations or guidance or changes in regulatory review for each submitted drug application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical studies, clinical trials or other studies and testing. In addition, varying interpretations of the data obtained from preclinical studies and clinical trials could delay, limit or prevent marketing approval of a drug candidate. Any marketing approval we, or any collaborators we may have in the future, ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved drug not commercially viable.

Any delay in obtaining or failure to obtain required approvals could materially adversely affect our ability or that of any collaborators we may have to generate revenue from the particular drug candidate, which likely would result in significant harm to our financial position and adversely impact our stock price.

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Failure to obtain marketing approval in international jurisdictions would prevent our drug candidates from being marketed abroad.

In order to market and sell our drugs in the European Union and many other jurisdictions, we, and any collaborators we may have in the future, must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The marketing approval process outside of the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside of the United States, it is required that the drug be approved for reimbursement before the drug can be approved for sale in that country. We, and any collaborators we may have in the future, may not obtain approvals from regulatory authorities outside of the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside of the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA.

Even if we, or any collaborators we may have in the future, obtain marketing approvals for our drug candidates, the terms of approvals and ongoing regulation of our drugs may limit how we, or they, manufacture and market our drugs, which could materially impair our ability to generate revenue.

Once marketing approval has been granted, an approved drug and its manufacturer and marketer are subject to ongoing review and extensive regulation. We, and any collaborators we may have in the future, must therefore comply with requirements concerning advertising and promotion for any of our drug candidates for which we or they obtain marketing approval. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the drug's approved labeling. Thus, we, and any collaborators we may have in the future, may not be able to promote any drugs we develop for indications or uses for which they are not approved.

In addition, manufacturers of approved drugs and those manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We, our contract manufacturers, our future collaborators and their contract manufacturers could be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMPs.

Accordingly, assuming we, or our future collaborators, receive marketing approval for one or more of our drug candidates, we, and our future collaborators, and our and their contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control.

If we, and our future collaborators, are not able to comply with post-approval regulatory requirements, we, and our future collaborators, could have the marketing approvals for our drugs withdrawn by regulatory authorities and our, or our future collaborators', ability to market any future drugs could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

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Any of our drug candidates for which we, or our future collaborators, obtain marketing approval in the future could be subject to post-marketing restrictions or withdrawal from the market and we, and our future collaborators, may be subject to substantial penalties if we, or they, fail to comply with regulatory requirements or if we, or they, experience unanticipated problems with our drugs following approval.

Any of our drug candidates for which we, or our future collaborators, obtain marketing approval in the future, as well as the manufacturing processes, post-approval studies and measures, labeling, advertising and promotional activities for such drug, among other things, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a drug candidate is granted, the approval may be subject to limitations on the indicated uses for which the drug may be marketed or to the conditions of approval, including the requirement to implement a Risk Evaluation and Mitigation Strategy, which could include requirements for a restricted distribution system.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of a drug. The FDA and other agencies, including the Department of Justice, or the DOJ, closely regulate and monitor the post-approval marketing and promotion of drugs to ensure that they are manufactured, marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we, or our future collaborators, do not market any of our drug candidates for which we, or they, receive marketing approval for only their approved indications, we, or they, may be subject to warnings or enforcement action for off-label marketing. Violation of the Federal Food, Drug, and Cosmetic Act and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations or allegations of violations of federal and state health care fraud and abuse laws and state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with our drugs or their manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

litigation involving patients taking our drug;

restrictions on such drugs, manufacturers or manufacturing processes;

restrictions on the labeling or marketing of a drug;

restrictions on drug distribution or use;

requirements to conduct post-marketing studies or clinical trials;

warning letters or untitled letters;

withdrawal of the drugs from the market;

refusal to approve pending applications or supplements to approved applications that we submit;

recall of drugs;

fines, restitution or disgorgement of profits or revenues;

suspension or withdrawal of marketing approvals;

damage to relationships with any potential collaborators;

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unfavorable press coverage and damage to our reputation;

refusal to permit the import or export of drugs;

drug seizure; or

injunctions or the imposition of civil or criminal penalties.

Recently-enacted and future legislation may increase the difficulty and cost for us and our future collaborators to obtain marketing approval of and commercialize our drug candidates and affect the prices we, or they, may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our drug candidates, restrict or regulate post-approval activities and affect our ability, or the ability of our future collaborators, to profitably sell any drugs for which we, or they, obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or our future collaborators, may receive for any approved drugs.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, changed the way Medicare covers and pays for pharmaceutical products and could decrease the coverage and price that we, or our future collaborators, may receive for any approved drugs. While the MMA only addresses drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payors.

More recently, in March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the PPACA.

Among the provisions of the PPACA of potential importance to our drug candidates are the following:

an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents;

an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;

expansion of healthcare fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers and enhanced penalties for non-compliance;

a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices;

extension of manufacturers' Medicaid rebate liability;

expansion of eligibility criteria for Medicaid programs;

expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;

new requirements to report financial arrangements with physicians and teaching hospitals;

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a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and

a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes have been proposed and adopted since the PPACA was enacted. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our drug candidates for which marketing approval is obtained.

We expect that the PPACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved drug. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue from sales of drugs, attain profitability, or commercialize our drug candidates.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our drug candidates, if any, may be. In addition, increased scrutiny by the United States Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us and our future collaborators to more stringent drug labeling and post-marketing testing and other requirements.

Our relationships with healthcare providers and physicians and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third party payors will play a primary role in the recommendation and prescription of any drugs for which we obtain marketing approval. Our future arrangements with third party payors, healthcare providers and physicians may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any drugs for which we obtain marketing approval. These include the following:

Anti-Kickback Statute the federal healthcare anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;

False Claims Act the federal False Claims Act imposes criminal and civil penalties, including through civil whistleblower or *qui tam* actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties, currently set at \$5,500 to \$11,000 per false claim;

HIPAA the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters, and, as amended by the

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Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms and technical safeguards, with respect to maintaining the privacy, security and transmission of individually identifiable health information;

Transparency Requirements federal laws require applicable manufacturers of covered drugs to report payments and other transfers of value to physicians and teaching hospitals; and

Analogous State and Foreign Laws analogous state and foreign fraud and abuse laws and regulations, such as state anti-kickback and false claims laws, can apply to sales or marketing arrangements and claims involving healthcare items or services and are generally broad and are enforced by many different federal and state agencies as well as through private actions.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not pre-empted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of drugs from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Our employees may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk of employee fraud or other misconduct, including intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, provide accurate information to the FDA or comparable foreign regulatory authorities, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

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If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or commercialization efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling certain drug candidates outside of the United States and require us to develop and implement costly compliance programs.

If we expand our operations outside of the United States, we must comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The creation and implementation of international business practices compliance programs is costly and such programs are difficult to enforce, particularly where reliance on third parties is required.

The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. The anti-bribery provisions of the FCPA are enforced primarily by the DOJ. The Securities and Exchange Commission, or SEC, is involved with enforcement of the books and records provisions of the FCPA.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we

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expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain drugs and drug candidates outside of the United States, which could limit our growth potential and increase our development costs.

The failure to comply with laws governing international business practices may result in substantial penalties, including suspension or debarment from government contracting. Violation of the FCPA can result in significant civil and criminal penalties. Indictment alone under the FCPA can lead to suspension of the right to do business with the U.S. government until the pending claims are resolved. Conviction of a violation of the FCPA can result in long-term disqualification as a government contractor. The termination of a government contract or relationship as a result of our failure to satisfy any of our obligations under laws governing international business practices would have a negative impact on our operations and harm our reputation and ability to procure government contracts. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

Governments outside of the United States tend to impose strict price controls, which may adversely affect our revenues from the sales of drugs, if any.

In some countries, particularly the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug. To obtain reimbursement or pricing approval in some countries, we, or our future collaborators, may be required to conduct a clinical trial that compares the cost-effectiveness of our drug to other available therapies. If reimbursement of our drugs is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed.

Risks Related To Employee Matters And Managing Growth

Our future success depends on our ability to retain our Chief Executive Officer, our President and Chief Scientific Officer and other key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on Michael Kauffman, M.D., Ph.D., our Chief Executive Officer, and Sharon Shacham, Ph.D., M.B.A., our President and Chief Scientific Officer, as well as the other principal members of our management and scientific teams. Although we have entered into formal employment agreements with Drs. Kauffman and Shacham, these agreements do not prevent them from terminating their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

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Michael Kauffman, M.D., Ph.D. and Sharon Shacham, Ph.D., M.B.A. are married. The separation or divorce of the couple in the future could adversely affect our business.

Dr. Kauffman, our Chief Executive Officer and member of our board of directors, and Dr. Shacham, our President and Chief Scientific Officer, are married. They are two of our executive officers and are a vital part of our operations. If they were to become separated or divorced or could otherwise not amicably work with each other, one of them may decide to cease his or her employment with us or it could negatively impact our working environment. Alternatively, their work performance may not be satisfactory if they become preoccupied with issues relating to their personal situation. In these cases, our business could be materially harmed.

We expect to expand our development, regulatory and future sales and marketing capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, regulatory affairs and, potentially, sales and marketing. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The physical expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Our business and operations may be materially adversely affected in the event of computer system failures.

Despite the implementation of security measures, our internal computer systems, and those of our contract research organizations and other third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, natural disasters, fire, terrorism, war and telecommunication and electrical failures. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our drug development programs. For example, the loss of clinical trial data from ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of our drug candidates could be delayed.

Risks Related To Our Common Stock And This Offering

Our executive officers, directors and principal stockholders maintain the ability to control all matters submitted to stockholders for approval.

As of March 14, 2014, our executive officers, directors and a small number of stockholders own more than a majority of our outstanding common stock. As a result, if these stockholders were to choose to act together, they would be able to control all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of voting power could delay or prevent an acquisition of our company on terms that other stockholders may desire.

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Provisions in our corporate charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our corporate charter and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

establish a classified board of directors such that not all members of the board are elected at one time;

allow the authorized number of our directors to be changed only by resolution of our board of directors;

limit the manner in which stockholders can remove directors from the board;

establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;

require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;

limit who may call stockholder meetings;

authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and

require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

If you purchase shares of common stock in this offering, you will suffer immediate dilution of your investment.

The price of our common stock in this offering will be substantially higher than the net tangible book value per share of our common stock. Therefore, if you purchase shares of our common stock in this offering, you will pay a price per share that substantially exceeds our net tangible book value per share after this offering. To the extent shares are issued under outstanding options, you will incur further dilution. Based on an assumed public offering price of \$ _____ per share, which is the last reported sale price of our common stock on _____, 2014, you will experience immediate dilution of \$ _____ per share, representing the difference between our as adjusted net tangible book value per share after giving effect to this offering and the assumed public offering price per share.

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An active trading market for our common stock may not be sustained following this offering.

Although our common stock is listed on The NASDAQ Global Select Market, an active trading market for our shares may not be sustained following this offering. If an active market for our common stock does not continue, it may be difficult for you to sell shares you purchase in this offering without depressing the market price for the shares, or at all. An inactive trading market for our common stock may also impair our ability to raise capital to continue to fund our operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

If securities analysts do not continue to publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline.

The trading market for our common stock relies in part on the research and reports that industry or financial analysts publish about us or our business. There can be no assurance that analysts will provide favorable coverage or continue to cover us. If one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

The price of our common stock has been and may be volatile in the future and fluctuate substantially.

Our stock price has been and is likely to be volatile and may fluctuate substantially. The stock market in general and the market for pharmaceutical and biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. The market price for our common stock may be influenced by many factors, including:

the success of competitive drugs or technologies;

results of clinical trials of our drug candidates or those of our competitors;

regulatory or legal developments in the United States and other countries;

developments or disputes concerning patent applications, issued patents or other proprietary rights;

the recruitment or departure of key personnel;

the level of expenses related to any of our drug candidates or clinical development programs;

the results of our efforts to discover, develop, acquire or in-license additional drug candidates or drugs;

actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;

variations in our financial results or those of companies that are perceived to be similar to us;

changes in the structure of healthcare payment systems;

market conditions in the pharmaceutical and biotechnology sectors;

general economic, industry and market conditions; and

the other factors described in this "Risk Factors" section.

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We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because pharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and our resources, which could harm our business.

We have broad discretion in the use of our cash and cash equivalents, including the net proceeds we receive in this offering, and may not use them effectively.

Our management has broad discretion to use our cash and cash equivalents, including the net proceeds we receive in this offering, to fund our operations and could spend these funds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our drug candidates. Pending their use to fund our operations, we may invest our cash and cash equivalents, including the net proceeds from this offering, in a manner that does not produce income or that loses value.

We are an "emerging growth company," and the reduced disclosure requirements applicable to emerging growth companies may make our common stock less attractive to investors.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company for up to five years. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, only two years of audited financial statements and a correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure, reduced disclosure obligations regarding executive compensation and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. In this report, we have not included, and will not include in our proxy statement, all of the executive compensation related information that would be required if we were not an emerging growth company. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

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We will continue to incur increased costs as a result of operating as a public company, and our management will need to continue to devote substantial time to compliance initiatives and corporate governance practices.

As a public company, and particularly after we are no longer an "emerging growth company," we will incur significant legal, accounting and other expenses. In addition, the Sarbanes-Oxley Act of 2002 and rules subsequently implemented by the SEC and NASDAQ have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to continue to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly.

We cannot predict with certainty the amount of additional costs we may incur to continue to operate as a public company, nor can we predict the timing of such costs; however, we estimate that our incremental costs resulting from operating as a public company may be between \$2.0 million and \$4.0 million per year. In addition, the rules and regulations applicable to public companies are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies which could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company, we are not required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we are engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. In the course of the preparation and external audit of our consolidated financial statements, we and our independent registered public accounting firm identified "significant deficiencies" in our internal control over financial reporting related to the lack of sufficient staff in our finance department to segregate accounting duties. A significant deficiency is a deficiency, or combination of deficiencies, in internal control over financial reporting that is less severe than a material weakness, yet important enough to merit attention by those responsible for oversight of a company's financial reporting. Following the identification of these control deficiencies, we took actions and measures to improve our internal control over financial reporting by hiring additional employees and consultants at various appropriate levels. Our remediation efforts may not, however, enable us to avoid material weaknesses or other significant deficiencies in the future. There is a risk that neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements. In addition, if we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, of our common stock will be the sole source of gain for our stockholders.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In

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addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be the sole source of gain for our stockholders for the foreseeable future.

A significant portion of our total outstanding shares are restricted from immediate resale but may be sold into the market in the near future, which could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. After this offering, we will have outstanding _____ shares of common stock based on 29,753,726 shares outstanding as of March 14, 2014. This includes the shares that we and the selling stockholders are selling in this offering, which may be resold in the public market immediately without restriction, unless purchased by our affiliates. Of the remaining shares, approximately 21.9 million shares are currently restricted as a result of securities laws or lock-up agreements entered into in connection with our initial public offering or this offering but will be able to be sold as described in the "Shares Eligible for Future Sale" and "Underwriting" sections of this prospectus. The restrictions under the 180-day lock-up arrangements with the underwriters for our initial public offering and under such option and restricted stock agreements are due to expire on May 4, 2014, resulting in these shares becoming eligible for public sale on May 5, 2014 if they are registered under the Securities Act of 1933, as amended (the "Securities Act"), or if they qualify for an exemption from registration under the Securities Act, including under Rules 144 or 701.

Moreover, holders of an aggregate of approximately 18.6 million shares of our common stock have rights, subject to some conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We also intend to register all shares of common stock that we may issue under our equity compensation plans. Once we register these shares, they can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates and the lock-up agreements described or this offering as described in the "Shares Eligible for Future Sale" and "Underwriting" sections of this prospectus.

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements that involve substantial risks and uncertainties. These statements include all matters that are not related to present facts or current conditions or that are not historical facts, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward- looking statements.

The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements include, among other things, statements about:

the timing, progress and results of current and future preclinical studies and clinical trials, and our research and development programs;

our plans to develop and commercialize our drug candidates;

the timing or likelihood of regulatory filings and approvals;

the implementation of our business model and strategic plans for our business, drug candidates and technology;

our commercialization, marketing and manufacturing capabilities and strategy;

the rate and degree of market acceptance and clinical utility of our drugs;

our competitive position;

our intellectual property position;

developments and projections relating to our competitors and our industry;

our ability to establish collaborations or obtain additional funding;

our expectations regarding the time during which we will be an emerging growth company under the JOBS Act;

our expectations related to the use of proceeds from this offering; and

our estimates regarding expenses, future revenue, capital requirements and needs for additional financing.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations

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disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this prospectus, particularly in the "Risk Factors" section, that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments that we may make.

You should read this prospectus, the documents that we reference in this prospectus and the documents that we have filed as exhibits to the registration statement of which this prospectus is a part completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements contained in this prospectus are made as of the date of this prospectus and we do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

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USE OF PROCEEDS

We estimate that the net proceeds to us from this offering will be approximately \$ _____ million, based on an assumed public offering price of \$ _____ per share, which is the last reported sale price of our common stock on _____, 2014, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their option to purchase additional shares of our common stock in full, we estimate that our net proceeds will be approximately \$ _____ million.

We will not receive any of the proceeds from the sale of shares in this offering by the selling stockholders.

As of December 31, 2013, we had cash and cash equivalents of \$156.0 million. We currently intend to use the net proceeds from this offering, together with our existing cash and cash equivalents, as follows:

approximately \$ _____ million to fund the continued clinical development of our lead drug candidate, Selinexor (KPT-330), including approximately \$ _____ million for initiating and conducting planned registration-directed clinical trials of Selinexor in three hematological malignancy indications, approximately \$ _____ million for initiating and conducting Phase 2 clinical trials of Selinexor in solid tumor indications; approximately \$ _____ million to fund additional clinical trials of Selinexor in additional cancer indications as a single agent as well as in combination with other therapies;

approximately \$ _____ million to continue our preclinical development of our drug candidates for anti-inflammatory, viral and wound-healing indications;

approximately \$ _____ million for discovery, research, preclinical development and clinical trials of additional drug candidates; and

the balance for working capital and other general corporate purposes.

This expected use of net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development, feedback from regulatory authorities, the status of and results from clinical trials, as well as any collaborations that we may enter into with third parties for our drug candidates, and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering.

Pending use of the proceeds as described above, we intend to invest the proceeds in a variety of capital preservation investments, including short-term, interest-bearing, investment-grade instruments and U.S. government securities.

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Our common stock began trading on The NASDAQ Global Select Market under the symbol "KPTI" on November 6, 2013. Prior to that time, there was no public market for our common stock. The following table sets forth the high and low sale prices per share of our common stock, as reported on The NASDAQ Global Select Market, for the periods indicated.

	High	Low
Year Ended December 31, 2013		
Fourth quarter (from November 6, 2013)	\$ 25.69	\$ 15.50
Year Ending December 31, 2014		
First quarter (through _____, 2014)	\$	\$

On _____, 2014, the last reported sale price of our common stock on The NASDAQ Global Select Market was \$ _____ per share. As of the date of this prospectus, we had approximately 43 holders of record of our common stock. This number does not include beneficial owners whose shares are held by nominees in street name.

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DIVIDEND POLICY

We have not declared or paid any cash dividends on our capital stock since our inception. We intend to retain future earnings, if any, to finance the operation and expansion of our business and do not anticipate paying any cash dividends in the foreseeable future.

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INDUSTRY AND OTHER DATA

We obtained the industry, market and competitive position data in this prospectus from our own internal estimates and research as well as from industry and general publications and research, surveys and studies conducted by third parties. Industry and general publications and research, surveys and studies conducted by third parties generally state that they have been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information.

Table of Contents**CAPITALIZATION**

The following table sets forth our cash and cash equivalents and capitalization as of December 31, 2013, as follows:

on an actual basis; and

on an as adjusted basis to give effect to our issuance and sale of _____ shares of common stock in this offering at an assumed public offering price of \$ _____ per share, which was the last reported sale price of our common stock on The NASDAQ Global Select Market on _____, 2014, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

You should read this information in conjunction with our consolidated financial statements and the related notes appearing at the end of this prospectus and the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section, the "Selected Consolidated Financial Data" section and other financial information contained in this prospectus.

	As of December 31, 2013	
	Actual (in thousands, except share and per share data)	As Adjusted
Cash and cash equivalents	\$ 155,974	\$
Undesignated preferred stock, \$0.0001 par value: 5,000,000 shares authorized and no shares issued or outstanding		
Common stock, par value \$0.0001 per share; 100,000,000 shares authorized, 29,587,258 shares issued and outstanding, actual; and _____ shares issued and outstanding, as adjusted		3
Additional paid-in capital	217,500	
Accumulated deficit	(62,569)	()
Total stockholders' equity (deficit)		154,934
Total capitalization	\$ 154,934	\$

The table above does not include:

166,949 shares of unvested restricted stock subject to repurchase by us;

2,410,522 shares of our common stock issuable upon exercise of stock options outstanding as of December 31, 2013 at a weighted-average exercise price of \$7.85 per share;

635,962 and 242,424 additional shares of our common stock available for future issuance, as of December 31, 2013, under our 2013 stock incentive plan and our 2013 employee stock purchase plan, respectively; and

1,190,149 additional shares of our common stock that became available for issuance under our 2013 stock incentive plan on January 1, 2014.

Table of Contents**DILUTION**

If you invest in our common stock in this offering, your ownership interest will be immediately diluted to the extent of the difference between the public offering price per share and the as adjusted net tangible book value per share of our common stock after this offering.

Our historical net tangible book value as of December 31, 2013 was approximately \$154.9 million, or \$5.21 per share of common stock. Our historical net tangible book value is the amount of our total tangible assets less our total liabilities. Historical net tangible book value per share is our historical net tangible book value divided by the number of shares of common stock outstanding as of December 31, 2013.

After giving effect to our sale of _____ shares of common stock in this offering at an assumed public offering price of \$ _____ per share, which was the last reported sale price of our common stock on The NASDAQ Global Select Market on _____, 2014, and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of December 31, 2013 would have been approximately \$ _____ million, or approximately \$ _____ per share. This amount represents an immediate increase in as adjusted net tangible book value of \$ _____ per share to our existing stockholders and an immediate dilution in as adjusted net tangible book value of approximately \$ _____ per share to new investors purchasing shares of common stock in this offering. We determine dilution by subtracting the as adjusted net tangible book value per share after giving effect to this offering from the assumed public offering price per share.

The following table illustrates this dilution:

Assumed public offering price per share	\$
Historical net tangible book value per share as of December 31, 2013	\$ 5.21
Increase per share attributable to this offering	

As adjusted net tangible book value per share after this offering

Dilution per share to new investors	\$
-------------------------------------	----

If the underwriters exercise their option to purchase additional shares of our common stock in this offering, or if additional shares of our common stock are issued in connection with the exercise of options, you will experience further dilution.

Table of Contents**SELECTED CONSOLIDATED FINANCIAL DATA**

You should read the following selected consolidated financial data in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and the related notes appearing elsewhere in this prospectus.

The consolidated statements of operations data for the years ended December 31, 2013, 2012 and 2011 and the consolidated balance sheet data as of December 31, 2011, 2012 and 2013 are derived from our audited consolidated financial statements appearing elsewhere in this prospectus. Our historical results are not necessarily indicative of the results to be expected in any future period.

	Year Ended December 31,			Period from
	2013	2012	2011	December 22, 2008 (Date of Inception) to December 31, 2013
(in thousands, except share and per share data)				
Consolidated Statement of Operations Data:				
Contract and grant revenue	\$ 387	\$ 634	\$ 152	\$ 1,266
Operating expenses:				
Research and development	28,452	14,095	8,623	52,835
General and administrative	5,885	2,429	1,840	10,817
Total operating expenses	34,337	16,524	10,463	63,652
Loss from operations	(33,950)	(15,890)	(10,311)	(62,386)
Interest income (expense), net	3	2		(183)
Net loss	\$ (33,947)	\$ (15,888)	\$ (10,311)	\$ (62,569)
Net loss per share applicable to common stockholders basic and diluted	\$ (5.59)	\$ (8.95)	\$ (10.27)	\$ (35.00)
Weighted-average number of common shares used in net loss per share applicable to common stockholders basic and diluted	6,067,679	1,775,323	1,004,144	1,787,668

2013 2012 2011
(in thousands)

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Consolidated Balance Sheet Data:

Cash and cash equivalents	\$ 155,974	\$ 391	\$ 6,512
Working capital	154,664	(976)	4,749
Total assets	158,226	1,311	7,224
Total preferred stock and preferred stock subscription		27,258	17,758
Total stockholders' equity (deficit)	154,934	(27,877)	(12,651)

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**MANAGEMENT'S DISCUSSION AND ANALYSIS OF
FINANCIAL CONDITION AND RESULTS OF OPERATIONS**

The following discussion and analysis of our financial condition and results of operations should be read together with our selected consolidated financial data and the consolidated financial statements and related notes included elsewhere in this prospectus. This discussion and analysis contains forward-looking statements that involve risks and uncertainties. As a result of many factors, such as those set forth under the section entitled "Risk Factors" and elsewhere in this prospectus, our actual results may differ materially from those anticipated in these forward-looking statements.

Overview

We are a clinical-stage pharmaceutical company founded in December 2008 by Dr. Sharon Shacham. We are focused on the discovery and development of novel first-in-class drugs directed against nuclear transport targets for the treatment of cancer and other major diseases. Our scientific expertise is focused on the understanding of the regulation of intracellular transport between the nucleus and the cytoplasm. We have discovered and developed novel, small molecule, **S**elective **I**nhibitors of **N**uclear **E**xport, or **SINE**, compounds that inhibit the nuclear export protein XPO1. We have worldwide rights to these SINE compounds. Our lead drug candidate, Selinexor (KPT-330), is an XPO1 inhibitor being evaluated in multiple open-label Phase 1 clinical trials in patients with heavily pretreated relapsed and/or refractory hematological and solid tumor malignancies. To date, we have administered Selinexor to over 240 patients in these trials. Preliminary evidence of anti-cancer activity has been observed in some patients and Selinexor has been sufficiently well-tolerated to allow many of these patients to remain on therapy for prolonged periods, including several who have remained on study for over 8-12 months. To our knowledge, no other XPO1 inhibitors are in clinical development at the present time.

We have devoted substantially all of our efforts to research and development. We expect that it will be several years, if ever, before we have a drug candidate ready for commercialization for the treatment of human disease. To date, we have financed our operations primarily with the net proceeds from the private placements of our preferred stock and the net proceeds from our initial public offering.

Since inception, we have incurred significant operating losses. Our net loss was \$33.9 million, \$15.9 million and \$10.3 million for the years ended December 31, 2013, 2012 and 2011, respectively. As of December 31, 2013, we had an accumulated deficit of \$62.6 million. We have not generated any revenue to date from sales of any drugs.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that our expenses will increase substantially if and as we:

continue our research and preclinical and clinical development of our drug candidates;

identify additional drug candidates;

initiate additional clinical trials for our drug candidates;

seek marketing approvals for any of our drug candidates that successfully complete clinical trials;

ultimately establish a sales, marketing and distribution infrastructure to commercialize any drugs for which we may obtain marketing approval;

maintain, expand and protect our intellectual property portfolio;

hire additional clinical, quality control and scientific personnel;

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acquire or in-license other drugs and technologies; and

add operational, financial and management information systems and personnel, including personnel to support our drug development, any future commercialization efforts and our operations as a public company.

Financial Overview

Revenue Recognition

To date, we have not generated any revenue from drug sales and do not expect to generate any revenue from drug sales for many years, if ever. Our ability to generate revenues from drug sales will depend on the successful development and eventual commercialization of our drug candidates.

To date, our only revenue is from foundation and government grants and contracts.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our drug discovery efforts, and the development of our drug candidates, which include:

employee-related expenses, including salaries, benefits, travel and stock-based compensation expense;

expenses incurred under agreements with third parties, including contract research organizations, contract manufacturing organizations and consultants that conduct clinical trials and preclinical studies;

the cost of acquiring, developing and manufacturing clinical trial materials;

facilities, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance, and other operating costs; and

costs associated with preclinical activities and regulatory operations.

Costs for certain development activities, such as clinical trials, are recognized based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations, or information provided to us by our vendors on their actual costs incurred. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the financial statements as prepaid or accrued research and development.

Since our research and development has been focused primarily on using our drug discovery and optimization platform to identify drug candidates, we have not historically tracked research and development costs by project. In addition, we use our employee and infrastructure resources across multiple research and development projects. We expect to track specific project costs when additional drug candidates enter clinical trials in humans.

The successful development of our drug candidates is highly uncertain. As such, at this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the remainder of the development of these drug candidates. We are also unable to predict when, if ever, material net cash inflows will commence from any drug candidates. This is due to the numerous risks and uncertainties associated with developing drugs, including the uncertainty of:

establishing an appropriate safety profile with IND-enabling toxicology studies;

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successful enrollment in, and completion of, clinical trials;

receipt of marketing approvals from applicable regulatory authorities;

establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;

obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our drug candidates;

launching commercial sales of the drugs, if and when approved, whether alone or in collaboration with others; and

maintaining a continued acceptable safety profile of the drugs following approval.

A change in the outcome of any of these variables with respect to the development of any of our drug candidates would significantly change the costs and timing associated with the development of that drug candidate.

Research and development activities are central to our business model. Drug candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect research and development costs to increase significantly for the foreseeable future as our drug candidates progress in clinical trials. However, we do not believe that it is possible at this time to accurately project total program-specific expenses through commercialization. There are numerous factors associated with the successful commercialization of any of our drug candidates, including future trial design and various regulatory requirements, many of which cannot be determined with accuracy at this time based on our stage of development. Additionally, future commercial and regulatory factors beyond our control will impact our clinical development programs and plans.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in executive, finance and administrative functions. Other significant costs include facility costs not otherwise included in research and development expenses, legal fees relating to patent and corporate matters and fees for accounting and consulting services.

We anticipate that our general and administrative expenses will increase in the future to support continued research and development activities, potential commercialization of our drug candidates and increased costs of operating as a public company. These increases will likely include increased costs related to the hiring of additional personnel and fees to outside consultants, lawyers and accountants, among other expenses. Additionally, we anticipate that the increased costs associated with being a public company will include expenses related to services associated with maintaining compliance with exchange listing and Securities and Exchange Commission requirements, insurance, and investor relations costs.

Critical Accounting Policies and Estimates

Our discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which we have prepared in accordance with United States generally accepted accounting principles. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported amounts of revenues and expenses during the reporting periods. On an ongoing basis, we evaluate our estimates and judgments, including those described in greater detail below. We base our

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estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements included elsewhere in this prospectus, we believe that the following accounting policies are the most critical to aid you in fully understanding and evaluating our financial condition and results of operations.

Accrued Research and Development Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing quotations and contracts, identifying services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. The significant estimates in our accrued research and development expenses include fees paid to contract research organizations, or CROs, and contract manufacturing organizations, or CMOs, in connection with research and development activities for which we have not yet been invoiced.

We base our expenses related to CROs and CMOs on our estimates of the services received and efforts expended pursuant to quotes and contracts with CROs and CMOs that conduct research and development on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the research and development expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepayment accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting amounts that are too high or too low in any particular period.

Stock-based Compensation

Since our initial public offering, the exercise price per share of all options grants has been set at the closing price of our common stock on the NASDAQ Global Select Market on the applicable date of grant, which our board of directors believes represents the fair value of our common stock.

Prior to becoming a public company in November 2013, we utilized significant estimates and assumptions in determining the fair value of our common stock. We granted stock options at exercise prices not less than the fair value of our common stock as determined by the board of directors, with input from management. The board of directors determined the estimated fair market value of our common stock based on a number of objective and subjective factors, including external market conditions affecting the biotechnology industry and prices at which we sold shares of convertible preferred stock, the superior rights and preferences of securities senior to our common stock at the time and the likelihood of achieving a liquidity event, such as an initial public offering.

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Prior to becoming a public company, we periodically determined for financial reporting purposes the estimated per share fair value of our common stock at various dates using contemporaneous valuations performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*, also known as the Practice Aid. In conducting the contemporaneous valuations, we considered all objective and subjective factors that we believed to be relevant for each valuation conducted, including our best estimate of our business condition, prospects and operating performance at each valuation date. Within the contemporaneous valuations performed, a range of factors, assumptions and methodologies were used. The significant factors included:

the prices of our preferred stock sold to or exchanged between outside investors in arm's length transactions, and the rights, preferences and privileges of our preferred stock as compared to those of our common stock, including the liquidation preferences of our preferred stock;

our results of operations, financial position and the status of research and development efforts;

the composition of, and changes to, our management team and board of directors;

the lack of liquidity of our common stock as a private company;

our stage of development and business strategy and the material risks related to our business and industry;

the valuation of publicly traded companies in the life sciences and biotechnology sectors, as well as recently completed mergers and acquisitions of peer companies;

any external market conditions affecting the life sciences and biotechnology industry sectors;

the likelihood of achieving a liquidity event for the holders of our common stock and stock options, such as an initial public offering, or a sale of our company, given prevailing market conditions; and

the state of the initial public offering market for similarly-situated privately-held biotechnology companies.

The dates of our contemporaneous valuations have not always coincided with the dates of our option grants. In determining the exercise prices of option grants, our board of directors considered, among other things, the most recent contemporaneous valuations of our common stock and our assessment of additional objective and subjective factors we believed were relevant as of the grant date. The additional factors considered when determining any changes in fair value between the most recent contemporaneous valuation and the grant dates included, when available, the prices paid in recent transactions involving our equity securities, as well as our stage of development, our operating and financial performance and current business conditions.

In July 2013, based on our review of overall market conditions and the improving market for biopharmaceutical initial public offerings, our board of directors determined that a significant shift was occurring with respect to the valuation we could achieve in an initial public offering and directed our management to begin the process of preparing our company for an initial public offering. We selected underwriters and held an organizational meeting in August 2013. We believe these events increased the probability of an initial public offering scenario and therefore, in connection with the preparation of our consolidated financial statements at such time, we re-assessed the fair value of our common stock for financial reporting purposes at interim dates between the contemporaneous valuations where there were stock option grants.

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On October 23, 2013, the pricing committee of our board of directors determined the estimated price range for our initial public offering, after consultation with the underwriters. The estimated price range that was determined by the pricing committee of our board of directors implied a higher initial public offering valuation than we used in our contemporaneous common stock valuations. In connection with the process of determining the estimated price range, we re-assessed the fair value of our common stock for financial reporting purposes through additional retrospective valuations.

We issue stock-based awards to employees and non-employees, generally in the form of stock options and restricted stock. We account for our stock-based awards in accordance with Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 718, *Compensation - Stock Compensation*, or ASC 718. ASC 718 requires all stock-based awards to employees, including grants of employee stock options and modifications to existing stock options, to be recognized in the consolidated statements of operations and comprehensive loss based on their fair values. We account for stock-based awards to non-employees in accordance with FASB ASC Topic 505-50, *Equity-Based Payments to Non-Employees*, which requires the fair value of the award to be re-measured at fair value as the award vests. We recognize the compensation cost of stock-based awards to employees on a straight-line basis over the vesting period of the award and by using an accelerated attribution model for awards to non-employees. Described below is the methodology we have utilized in measuring stock-based compensation expense.

We estimate the fair value of our options to employees and non-employees using the Black-Scholes option pricing model, which requires the input of highly subjective assumptions, including (a) the expected volatility of our stock, (b) the expected term of the option, (c) the risk-free interest rate, and (d) expected dividends. Since there was no public market for our common stock prior to our initial public offering, we lacked company specific historical and implied volatility data. In addition, as a newly public company, we do not have sufficient history to estimate the volatility of our common stock price or the expected life of the options. Therefore, we base our estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. For these analyses, we select companies with comparable characteristics to ours including enterprise value, risk profiles, position within the industry, and with historical share price information sufficient to meet the expected term of the options. We compute the historical volatility data using the closing prices for the selected companies' shares during the equivalent period of the calculated expected term of our options. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available. We estimate the expected term of our employee stock options using the "simplified" method, whereby the expected term equals the average of the vesting term and the original contractual term of the option. For non-employee stock options, we utilize the contractual term of the option. The risk-free interest rates for periods within the expected term of the option are based on the U.S. Treasury yield curve in effect during the period the options were granted. We have not paid and do not anticipate paying cash dividends on our shares of common stock; therefore, the expected dividend yield is assumed to be zero.

We are also required to estimate forfeitures at the time of grant, and revise those estimates in subsequent periods if actual forfeitures differ from estimates. We use historical data to estimate pre-vesting option forfeitures and record stock-based compensation expense only for those options that are expected to vest. To the extent that actual forfeitures differ from our estimates, the difference is recorded as a cumulative adjustment in the period the estimates were revised. Stock-based compensation expense recognized in the financial statements is based on options that are ultimately expected to vest.

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We have computed the fair value of employee and non-employee stock options at date of grant using the following assumptions:

	Year Ended December 31,					
	2013		2012		2011	
Expected volatility	85%	93%	79%	92%	78%	79%
Expected term (in years)	6.25	10	6.25	10	6.25	10
Risk-free interest rate	1.07%	3.01%	0.85%	1.76%	1.18%	2.62%
Expected dividend yield	0.0%		0.0%		0.0%	

The weighted average grant date fair value per share was \$11.09 for options granted during the year ended December 31, 2013, \$1.19 for options granted during the year ended December 31, 2012 and \$0.10 for options granted during the year ended December 31, 2011.

We recognized total stock-based compensation expense of approximately \$3.8 million during the year ended December 31, 2013, \$653,000 during the year ended December 31, 2012 and \$24,000 during the year ended December 31, 2011.

We had total unrecognized compensation cost related to unvested share based compensation arrangements of \$21.2 million as of December 31, 2013 and \$731,000 as of December 31, 2012. We expect to recognize this cost as compensation expense over the weighted average remaining service period of approximately 3.7 years.

Results of Operations

The following table summarizes our results of operations for the years ended December 31, 2013, 2012 and 2011:

	Years Ended December 31,		
	2013	2012	2011
	(in thousands)		
Contract and grant revenue	\$ 387	\$ 634	\$ 152
Operating expenses:			
Research and development	28,452	14,095	8,623
General and administrative	5,885	2,429	1,840
Loss from operations	(33,950)	(15,890)	(10,311)
Interest income	3	2	
Net loss	\$ (33,947)	\$ (15,888)	\$ (10,311)

Comparison of Years Ended December 31, 2013 and 2012

Contract and Grant Revenue. Contract and grant revenue decreased by \$247,000 to \$387,000 in 2013 from \$634,000 in 2012. The decrease in revenue was the result of recognizing fewer milestones during 2013 associated with a grant.

Research and Development Expense. Research and development expense increased by \$14.4 million to \$28.5 million in 2013 from \$14.1 million in 2012. The \$14.4 million increase is primarily related to:

an increase of \$8.3 million in clinical trial costs, including a \$3.2 million increase in the cost of the active pharmaceutical ingredient and finished drug product,

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an increase of \$2.7 million in consulting fees, including a \$1.5 million increase in stock-based compensation expense related to equity grants to consultants, primarily due to the higher fair value of our common stock,

an increase of \$1.5 million in personnel costs, primarily due to increased headcount and a \$447,000 increase in stock-based compensation expense related to equity grants to personnel, primarily related to the higher fair value of our common stock, and

an increase of \$1.4 million in discovery work, including preclinical studies and screening.

General and Administrative Expense. General and administrative expense increased by \$3.5 million to \$5.9 million for 2013 from \$2.4 million for 2012. The \$3.5 million increase is primarily related to:

an increase of \$1.2 million in consulting fees, primarily related to business development, investor relations and financial services, including a \$546,000 increase in stock-based compensation expense related to equity grants to consultants, primarily due to the higher fair value of our common stock,

an increase of \$1.1 million in personnel costs, primarily due to increased headcount and an increase of \$623,000 in stock-based compensation expense related to equity grants to personnel,

an increase of \$725,000 in professional fees, primarily related to higher corporate legal fees and audit fees,

an increase of \$138,000 in insurance expense, primarily due to our becoming a publicly traded company, and

an increase of \$108,000 in travel expenses.

Comparison of Years Ended December 31, 2012 and 2011

Contract and Grant Revenue. Contract and grant revenue increased by \$482,000 to \$634,000 in 2012 from \$152,000 in 2011. The increase in revenue was the result of a full year of revenue recognized in 2012 associated with a grant.

Research and Development Expense. Research and development expense increased by \$5.5 million to \$14.1 million in 2012 from \$8.6 million in 2011. The \$5.5 million increase is primarily related to:

an increase of \$2.8 million in clinical trial costs, including a \$1.6 million increase in the cost of the active pharmaceutical ingredient and finished drug product,

an increase of \$966,000 in consulting fees, including a \$536,000 increase in stock-based compensation expense related to equity grants to consultants, primarily due to the higher fair value of our common stock,

an increase of \$669,000 in personnel costs, primarily due to increased headcount,

an increase of \$663,000 in collaboration expense, and

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an increase of \$586,000 in discovery work, including preclinical studies and screening, which reflects a \$371,000 decrease in outsourced medicinal chemistry.

These increases are partially offset by a \$373,000 decrease in toxicology and efficacy studies.

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General and Administrative Expense. General and administrative expense increased by \$589,000 to \$2.4 million for 2012 from \$1.8 million for 2011. The \$589,000 increase is primarily related to:

an increase of \$324,000 in professional fees, primarily related to higher legal fees related to protecting our intellectual property, as well as higher corporate legal fees and audit fees,

an increase of \$80,000 in personnel costs, primarily due to higher bonuses,

an increase of \$57,000 in occupancy expenses due to higher rent expense, and

an increase of \$57,000 in consulting fees, primarily related to business development, investor relations and financial services.

Liquidity and Capital Resources

To date, we have not generated any material revenues. We have financed our operations to date primarily through private placements of our preferred stock and proceeds from our initial public offering. As of December 31, 2013, we had \$156.0 million in cash and cash equivalents. As of December 31, 2013, we had received \$98.8 million in proceeds from the sale and issuance of preferred stock and \$113.2 million in net proceeds from our initial public offering. We expect that our existing cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements into early 2016.

Cash flows

The following table provides information regarding our cash flows:

	Years Ended December 31,		
	2013	2012	2011
	(in thousands)		
Net cash used in operating activities	\$ (30,290)	\$ (15,509)	\$ (8,549)
Net cash used in investing activities	(57)	(121)	(376)
Net cash provided by financing activities	185,930	9,509	11,992
Net increase (decrease) in cash and cash equivalents	\$ 155,583	\$ (6,121)	\$ 3,067

Net Cash Used in Operating Activities

Net cash used in operating activities was \$30.3 million during the year ended December 31, 2013 compared to \$15.5 million during the year ended December 31, 2012. The increase in cash used in operating activities during the year ended December 31, 2013 was driven primarily by an increase in our net loss and by changes in components of working capital, including an increase in prepaid expenses and other current assets.

Net cash used in operating activities was \$15.5 million for the year ended December 31, 2012 compared to \$8.5 million for the year ended December 31, 2011. The increase in cash used in operating activities during the year ended December 31, 2012 was driven primarily by an increase in our net loss and by changes in components of working capital, including a decrease in accounts payable and accrued expenses.

Net Cash Used in Investing Activities

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Net cash used in investing activities was \$57,000 during the year ended December 31, 2013 compared to \$121,000 during the year ended December 31, 2012. The cash used in investing activities was for the purchase of property and equipment.

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Net cash used in investing activities was \$121,000 during the year ended December 31, 2012 compared to \$376,000 during the year ended December 31, 2011. The cash used in investing activities was for the purchase of property and equipment.

Net Cash Provided by Financing Activities

Net cash provided by financing activities was \$185.9 million during the year ended December 31, 2013 compared to \$9.5 million during the year ended December 31, 2012. The increase in cash provided by financing activities during the year ended December 31, 2013 was driven primarily by the proceeds from the sale of preferred stock and proceeds from our initial public offering.

Net cash provided by financing activities was \$9.5 million during the year ended December 31, 2012 compared to \$12.0 million during the year ended December 31, 2011. The cash provided by financing activities for both periods was primarily from proceeds from the sale of preferred stock and issuance of the preferred stock subscriptions.

Funding requirements

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the clinical trials of, and assuming positive results of our clinical trials and based on regulatory feedback, if and when we seek marketing approval for, Selinexor and our other drug candidates. In addition, if we obtain marketing approval for any of our drug candidates, we expect to incur significant commercialization expenses related to drug sales, marketing, manufacturing and distribution to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of any collaborator that we may have at such time for any such drug. Furthermore, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts.

We expect that our existing cash and cash equivalents will enable us to fund our current operating plan and capital expenditure requirements into early 2016. Our future capital requirements will depend on many factors, including:

the progress and results of our current and planned clinical trials of Selinexor;

the scope, progress, results and costs of drug discovery, preclinical development, laboratory testing and clinical trials for our other drug candidates;

the costs, timing and outcome of regulatory review of our drug candidates;

our ability to establish and maintain collaborations on favorable terms, if at all;

the success of any collaborations that we may enter into with third parties;

the extent to which we acquire or in-license other drugs and technologies;

the costs of future commercialization activities, including drug sales, marketing, manufacturing and distribution, for any of our drug candidates for which we receive marketing approval, to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of any collaborator that we may have at such time;

the amount of revenue, if any, received from commercial sales of our drug candidates, should any of our drug candidates receive marketing approval; and

the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims.

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Identifying potential drug candidates and conducting preclinical studies and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve drug sales. In addition, our drug candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of drugs that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans.

Contractual Obligations

As of December 31, 2013, we had the following contractual obligations:

Contractual Obligations	Payments Due by Period			
	Total	2014	2015	2016 and beyond
	(in thousands)			
Operating lease obligations(1)	\$ 106	\$ 98	\$ 8	
Purchase obligations(2)				
Total contractual cash obligations	\$ 106	\$ 98	\$ 8	

(1) Represents future minimum lease payments under our non-cancelable operating lease.

(2) We enter into agreements in the normal course of business with CROs and CMOs for clinical trials and clinical supply manufacturing and with vendors for preclinical research. We have not included these payments in the table of contractual obligations above since the contracts are cancelable at any time by us, generally upon 30 days prior written notice to the vendor.

Royalty payments associated with our agreements have not been included in the above table of contractual obligations as we cannot reasonably estimate if or when they will occur. At this time, no royalty payments are probable of occurrence.

Multiple Myeloma Research Foundation

In July 2011, we entered into a research agreement with the Multiple Myeloma Research Foundation, or MMRF, for the research and development of small molecule XPO1 inhibitor compounds for the treatment of multiple myeloma. Pursuant to the research agreement, MMRF awarded us a \$1 million grant, all of which has been paid to us based on our achievement of specified milestones. We own all inventions and other intellectual property that arose or will arise from the conduct of the research program, which we refer to as program inventions and program intellectual property, respectively.

If we, our affiliates, licensees or transferees commercialize products incorporating a program invention or program intellectual property, which we call research program products, we would be obligated to pay to MMRF mid-single-digit royalties as a percentage of worldwide net sales of research program products, including Selinexor, sold by us, our affiliates, licensees or transferees. If we out-license rights to a research program product, we are obligated to pay MMRF a percentage of certain payments we receive from our licensee for the grant of such rights. If we sell all or substantially all of our assets to one or more third parties who were not our stockholders on the effective date of the agreement, or if one or more third parties acquire more than fifty percent of our equity and

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payments are made directly to our stockholders for the sale of their shares of our stock, each of which we call a change of control, we will be obligated to pay to MMRF a percentage of the value we or our shareholders receive in connection with such change of control. The maximum aggregate amount we may be obligated to pay to MMRF for royalties, out-licensing our rights or as a result of a change of control is \$6 million.

While this agreement has expired in accordance with its terms, our payment obligations survive the expiration of the agreement.

Off-Balance Sheet Arrangements

We did not have, during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under applicable Securities and Exchange Commission rules.

Inflation

We do not believe that inflation has had a significant impact on our revenues or results of operations since inception.

Table of Contents**BUSINESS****Overview**

We are a clinical-stage pharmaceutical company founded in December 2008 by Dr. Sharon Shacham. We are focused on the discovery and development of novel first-in-class drugs directed against nuclear transport targets for the treatment of cancer and other major diseases. Our scientific expertise is focused on the understanding of the regulation of intracellular transport between the nucleus and the cytoplasm. We have discovered and developed wholly-owned, novel, small molecule, **Selective Inhibitors of Nuclear Export**, or **SINE**, compounds that inhibit the nuclear export protein XPO1. Our lead drug candidate, Selinexor (KPT-330), is an XPO1 inhibitor being evaluated in multiple open-label Phase 1 clinical trials in patients with heavily pretreated relapsed and/or refractory hematological and solid tumor malignancies. To date, we have administered Selinexor to over 240 patients in these trials. Preliminary evidence of anti-cancer activity has been observed in some patients and Selinexor has been sufficiently well-tolerated to allow many of these patients to remain on therapy for prolonged periods, including several who have remained on study for over 8-12 months. We plan to initiate three clinical trials during 2014 designed to potentially serve as the basis for an application seeking regulatory approval for Selinexor in hematological malignancy indications. To our knowledge, no other XPO1 inhibitors are in clinical development at the present time.

The nucleus contains a cell's genetic material, or DNA, and acts as the control center of the cell, while the cytoplasm is the intracellular compartment around the nucleus where numerous processes involving proteins and other molecules occur. One of the ways in which the cell regulates the function of a particular protein is by controlling the protein's location within the cell, as a specific function may only occur within a particular location. In healthy cells, nuclear transport, both into and out of the nucleus, is a normal and regular occurrence that is tightly regulated and requires specific carrier proteins to occur. There are seven known nuclear export proteins (Exportins 1 through 7), of which the most well-characterized is Exportin 1, or XPO1, also known as CRM1. XPO1 mediates the export of approximately 220 different mammalian cargo proteins, including the vast majority of tumor suppressor proteins. Moreover, XPO1 appears to be the only nuclear exporter for most of these tumor suppressor proteins. Tumor suppressor proteins are anti-cancer proteins which must be in the nucleus to carry out their main function of detecting damage to genetic material that may indicate cancer, and, subsequently, initiating programmed cell death, or apoptosis, of the damaged cells. Cancer cells have increased levels of XPO1, causing the increased export of these tumor suppressor proteins from the nucleus, and thus counteracting the natural apoptotic process that protects the body from cancer. Due to XPO1 inhibition by our SINE compounds, the export of tumor suppressor proteins is prevented, thereby leading to their accumulation in the nucleus. The accumulation of tumor suppressor proteins in the nucleus reinitiates and amplifies their natural apoptotic function in cancer cells. This leads to the death of cancer cells through apoptosis with minimal effects on normal cells.

We are focused on building a leading oncology business. We were founded in December 2008 by Dr. Sharon Shacham, who established the Company to focus on the discovery and development of small molecule inhibitors of nuclear export. Dr. Shacham has led our company since its inception, and now serves as our President and Chief Scientific Officer, and co-chair of our Scientific Advisory Board. Her computational drug discovery algorithms formed a critical part of the technological basis for our drug discovery and optimization platform, which was used for the discovery of Selinexor, our lead drug candidate. Dr. Shacham has played a leadership role in the discovery and development of many novel drug candidates, which have been or are being tested in human clinical trials, prior to her founding of Karyopharm and while at Karyopharm. Along with Dr. Shacham, we are led by Dr. Michael Kauffman, M.D., Ph.D., who joined the Company in January 2011 and now serves as our Chief Executive Officer. Dr. Kauffman played a leadership role in the development and approval of Velcade® at Millenium Pharmaceuticals, and of Kyprolis® while serving as Chief Medical Officer at Proteolix and then Onyx Pharmaceuticals.

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We believe that the XPO1-inhibiting SINE compounds that we have discovered and developed to date, including Selinexor, have the potential to provide a novel targeted therapy that enable tumor suppressor proteins to remain in the nucleus and promote apoptosis of cancer cells. Moreover, our SINE compounds spare normal cells, which, unlike cancer cells, do not have significant damage to their genetic material, and we believe this selectivity for cancer cells minimizes side effects. We believe that the oral administration of Selinexor and the lack of cumulative or major organ toxicities observed to date in patients treated with Selinexor in our Phase 1 clinical trials create the potential for its broad use across many cancer types, including both hematological and solid tumor malignancies. We believe that no currently approved cancer treatments or current clinical-stage cancer drug candidates are selectively targeting the restoration and increase in the levels of multiple tumor suppressor proteins in the nucleus.

We are currently conducting three open-label Phase 1 clinical trials of Selinexor, the first in patients with various advanced hematological malignancies, the second in patients with various advanced or metastatic solid tumor malignancies and the third, a food effect study, in patients who have metastatic, locally advanced or locally recurrent soft tissue or bone sarcomas. In these trials, we have observed preliminary evidence of anti-cancer activity of Selinexor across a spectrum of patients with advanced cancers who had received multiple previous treatments and, despite these treatments, had disease that was progressing at the time of enrollment in our clinical trials. Assuming continued positive results from our ongoing Phase 1 clinical trials of Selinexor and pending regulatory feedback, we plan to initiate registration-directed clinical trials of Selinexor in three hematological malignancy indications during 2014. We refer to these trials as registration-directed because they are designed to potentially serve as the basis for an application seeking regulatory approval of Selinexor. We expect to initiate registration-directed clinical trials for Selinexor in acute myeloid leukemia, or AML, in the first half of 2014, in diffuse large B-cell lymphoma, or DLBCL, in late summer 2014 and in Richter's Syndrome during the middle of 2014. We plan to seek regulatory approvals of Selinexor in North America and Europe in each such indication with respect to which we receive positive clinical trial results and positive regulatory feedback. We may seek such approvals in other geographies as well. In solid tumor malignancies, we have initiated Phase 2 clinical trials of Selinexor in relapsed glioblastoma multiforme and in ovarian, cervical and uterine carcinomas and expect to initiate Phase 2 clinical trials in squamous head, neck or lung cancers and hormone and chemotherapy refractory metastatic prostate cancer during 2014. As we continue to review response data in solid tumor and other hematological malignancies, including multiple myeloma, we may decide to initiate registration-directed trials in additional cancer indications. We intend to enter into collaborations for marketing and commercialization of Selinexor in particular geographies at an appropriate time.

We designed our Phase 1 clinical trials of Selinexor in relapsed and/or refractory hematological malignancies and relapsed and/or refractory solid tumor malignancies to evaluate the safety of Selinexor, to determine the Phase 2 clinical trial dose and dosing schedule and to evaluate preliminary anti-cancer activity of Selinexor. In patients evaluated in our hematological malignancy trial as of December 4, 2013, we have observed complete responses or remissions, partial responses or remissions, minimal responses or stable disease, all as determined in accordance with commonly accepted evaluation criteria for the specific indication. For example, partial or minimal responses or stable disease have been observed in 82% of patients with relapsed and/or refractory chronic B-cell malignancies. In patients with relapsed and/or refractory acute myeloid leukemia, we have observed complete remissions, partial remission, morphologic leukemia-free state or stable disease in 52% of patients, some for longer than three months. In 48% of patients in the solid tumor malignancy trial evaluated as of December 24, 2013, we have observed partial responses or stable disease, all as determined in accordance with Response Evaluation Criteria In Solid Tumors, or RECIST.

In addition to cancer, we believe that our SINE compounds have the potential to provide therapeutic benefit in a number of additional indications, including autoimmune and inflammatory

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diseases, wound healing, HIV and influenza. We have discovered and are developing a pipeline of SINE compounds that have shown evidence of activity in preclinical models of inflammation, wound healing and viral infection. We may seek to enter into development, marketing and commercialization collaboration arrangements for our SINE compounds other than Selinexor in non-oncology indications globally.

The table below summarizes the current stages of development of our key drug candidates and indications for which clinical trials are currently being conducted or indications that we expect to initially focus on for each candidate. We expect to initiate the planned clinical trials of Selinexor described below assuming continued positive results from our ongoing Phase 1 clinical trials and pending regulatory feedback. We also expect a number of investigator-sponsored trials, or ISTs, to be initiated for Selinexor in a variety of cancer indications in 2014. These ISTs could consist of single agent or combination studies with other agents in both hematological and solid tumor malignancies.

In addition, we conducted a Phase 2b clinical trial of Verdinexor (KPT-335), a SINE compound that is closely-related to Selinexor, in pet dogs with newly-diagnosed or first relapse after chemotherapy lymphomas. Our Phase 2b clinical trial is intended to support regulatory approval under the MUMS designation. We submitted the safety and effectiveness sections of a New Animal Drug Application to the U.S. Food and Drug Administration for regulatory approval in such indication in December 2013 and, if we obtain such approval, we plan to seek to enter into a collaboration with respect to the commercialization of Verdinexor.

The development of Selinexor, and our other drug candidates, including our other SINE compounds and PAK4 inhibitors, as well as Verdinexor, began with our proprietary drug discovery and optimization platform. We intend to continue using this platform, which includes expertise in computational chemistry, our proprietary virtual chemical library and *in silico* screening know-how, certain biochemical assays and *in silico* complexes of the structures of the target proteins bound with our small molecules, and other trade secrets and know-how, for the discovery and optimization of additional drug candidates for cancer and other major diseases.

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Our Strategy

As a clinical-stage pharmaceutical company focused on the discovery and development of orally available, novel first-in-class drugs directed against nuclear transport targets for the treatment of cancer and other major diseases, the critical components of our business strategy are to:

Develop and Seek Regulatory Approval of Selinexor, Our Novel Lead Drug Candidate, in North America and Europe. Assuming continued positive results from our ongoing Phase 1 and Phase 2 clinical trials of Selinexor and pending regulatory feedback, we plan to initiate registration-directed clinical trials of Selinexor in three hematological malignancy indications during 2014. We expect to initiate these clinical trials for Selinexor in AML, DLBCL and Richter's Syndrome. We plan to seek regulatory approvals of Selinexor in North America and Europe in each such indication with respect to which we receive positive clinical trial results and positive regulatory feedback. We may seek such approvals in other geographies as well. In solid tumor malignancies, we have initiated Phase 2 clinical trials of Selinexor in relapsed glioblastoma multiforme and in ovarian, cervical and uterine carcinomas and expect to initiate Phase 2 clinical trials in squamous head, neck or lung cancers and hormone and chemotherapy refractory metastatic prostate cancer during 2014.

Maximize the Commercial Value of Selinexor. We currently have global development, marketing and commercialization rights for Selinexor and we expect that we will continue to develop and seek regulatory approval for its use in oncology indications without a collaborator in North America and Europe. As we further develop Selinexor for oncology indications, we intend to evaluate marketing and commercialization opportunities. We intend to enter into collaborations for further development, marketing and commercialization of Selinexor in particular geographies outside of North America and Europe at an appropriate time.

Maintain our Competitive Advantage and Scientific Expertise in the Field of Nuclear Transport. We plan to continue to conduct research in the field of nuclear transport to further our understanding of the role it plays in the underlying biology of cancer, as well other major diseases. We also plan to continue fostering relationships with top scientific advisors and physicians. We believe that investing in the recruitment of exceptional advisors, employees and management is critical to our continued leadership in the nuclear transport field.

Develop Novel Drug Candidates By Leveraging Our Proprietary Drug Discovery and Optimization Platform and Our Understanding of Nuclear Transport. To date, we have identified Selinexor, other SINE compounds including KPT-350, a series of PAK4 inhibitors and Verdinexor through our drug discovery and optimization platform. We plan to continue to leverage our understanding of nuclear transport and our platform in our efforts to discover additional drug candidates in the form of specific nuclear transport inhibitors that promote the death of diseased cells while sparing normal cells.

Collaborate with Key Opinion Leaders to Conduct Investigator-Sponsored Trials of Selinexor. A significant part of our strategy for efficiently understanding the breadth of activity of Selinexor alone or in combination with other anti-cancer drugs includes the initiation of investigator-sponsored trials. We plan to facilitate the investigation of the breadth of the clinical activity of Selinexor through our established network of scientific advisors and physicians.

Maximize the Value of Our Other SINE Compounds in Non-Oncology Indications through Collaborations. We may seek to enter into development, marketing and commercialization collaboration arrangements for our other SINE compounds in non-oncology indications globally.

Table of Contents**Our Focus: Nuclear Transport**

A human cell is divided into various compartments, including the nucleus and the cytoplasm. The nucleus contains a cell's genetic material, or DNA, and is the compartment where gene expression and consequently cellular function is regulated. The cytoplasm is the compartment around the nucleus where translation of gene transcripts, or mRNA, to proteins, assembly of proteins into cellular structural elements, and cellular metabolism of fats, carbohydrates, and proteins, occur. One of the ways in which the cell regulates the function of a particular protein is by controlling the protein's location within the cell, as a specific function may only occur within a particular location. Certain proteins, including tumor suppressor proteins and other growth regulatory proteins, need to be transported from the cytoplasm, where they are made, into the nucleus where they need to be located for their primary functions to occur. The nuclear pore is a complex gate between the nucleus and cytoplasm, closely regulating the import and export of most large molecules, called macromolecules, including many proteins, into and out of the nucleus. In healthy cells, nuclear transport processes of macromolecules in either direction through the nuclear pore are tightly regulated and require specific carrier proteins, including nuclear export proteins, to occur. There are seven known nuclear export proteins. The most well-characterized was discovered in 1999 and is called Exportin 1, or XPO1 (also called CRM1). XPO1 mediates the export of approximately 220 different mammalian cargo proteins, including some growth regulatory proteins and the vast majority of tumor suppressor proteins. Moreover, XPO1 appears to be the only nuclear exporter for most of these tumor suppressor proteins, including those generally referred to as p53, p73, FOXO, pRB, BRCA1 and PP2A.

Cancer is a disease characterized by unregulated cell growth. Cancer typically develops when DNA in normal cells begins to fail and genes that regulate cell growth become disrupted. Tumor suppressor proteins are an integral part of the body's natural defense mechanism in identifying and preventing cancer. They exert their effects on cancer cells once DNA damage is detected by promoting apoptosis. Tumor suppressor proteins can also have an anti-cancer effect by dampening unregulated cell growth and division. In addition to tumor suppressor proteins, cells contain growth regulatory proteins that, when located in the nucleus, are involved in ensuring that cells undergo cell division, or cell growth, only under appropriate circumstances, such as repairing wounds, increasing cell numbers to deal with damage to an organ, or replacing cells that have died through normal circumstances. Growth regulatory proteins are also exported from the nucleus by XPO1 in all cells. Examples of well-characterized growth regulatory proteins are p21, p27 and E2F4.

XPO1 is also the only exporter of the anti-inflammatory protein I κ B, the inhibitor of NF- κ B. NF- κ B is known to play a role in cancer metastasis and resistance to chemotherapy as well as in many inflammatory and autoimmune diseases. Blockade of XPO1 leads to accumulation of I κ B in the cell nucleus where it binds to and inhibits NF- κ B. In this way, the inhibition of NF- κ B may be beneficial in overcoming chemotherapy resistance and in treating autoimmune diseases.

Because tumor suppressor proteins need to be located in the nucleus in order to carry out their anti-cancer activities, their nuclear export, or exit from the nucleus, leads to their being unavailable in the nucleus to identify cancer cells and initiate their death. As XPO1 levels have been shown to be elevated by two- to four-fold in nearly all cancer cells compared to their normal cell counterparts, it appears that cancer cells have co-opted XPO1 to move tumor suppressor proteins out of the nucleus, thereby adversely affecting their ability to identify and initiate the death of cancer cells. Increased levels of XPO1 in cancer cells also lead to excessive nuclear export of growth regulatory proteins and allow cancer cells to divide continuously and inappropriately. Higher levels of XPO1

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expression are also generally correlated with poor prognosis and/or resistance to chemotherapies. The figure below depicts the process by which XPO1 mediates the nuclear transport process.

XPO1 Mediation of Nuclear Transport

Our Approach: Targeting Nuclear Export with Selective Inhibitors of Nuclear Export, or SINE

Since the discovery of XPO1, a growing body of research has documented that the high levels of XPO1 found in cancer cells are associated with the transport of tumor suppressor proteins and growth regulatory proteins from their site of action in the nucleus into the cytoplasm, where their anti-cancer activity is minimal and they are ultimately degraded. The inhibition of XPO1 cargo binding has been studied for over ten years. XPO1 inhibitors block the nuclear export of tumor suppressor proteins and growth regulatory proteins, leading to accumulation of these proteins in the nucleus and enhancing their anti-cancer activity in the cell. The forced nuclear retention of these proteins can counteract a multitude of the oncogenic pathways that allow cancer cells with severe DNA damage to continue to grow and divide in an unrestrained fashion. One naturally occurring XPO1 inhibitor called leptomycin B has been shown to have potent anti-cancer activity *in vitro*, but has been toxic to normal cells. These toxicities to normal cells have been observed in both animals and humans, which we believe are most likely caused by the *irreversible* nature of leptomycin B binding to XPO1. Because of its observed toxicities in animals and humans, to our knowledge, leptomycin B is no longer being developed.

Our lead drug candidates are first-in-class, oral **Selective Inhibitors of Nuclear Export**, or **SINE**, compounds. We have discovered SINE compounds by applying our proprietary drug discovery

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and optimization platform to the recently published X-ray structure of XPO1. SINE compounds inhibit XPO1-mediated nuclear-cytoplasmic transport by *transiently* binding to the XPO1 cargo binding site, meaning that they block XPO1 cargo binding over an extended period of time, but do not permanently do so. Transient XPO1 inhibition, or inhibition of approximately 12 to 24 hours, which corresponds to the inhibition period that we have observed to date with our SINE compounds, appears to be sufficient for nuclear retention and the increase of tumor suppressor proteins in the nucleus. During this period, the inhibition of XPO1 cargo binding enables tumor suppressor proteins to accumulate in the nucleus of cancer cells and perform their normal role of detecting DNA damage, thereby inhibiting a cancer cell's ability to divide and promoting apoptosis. Healthy cells also build up tumor suppressor proteins in the presence of a SINE compound, but are able to resume normal activity after transient XPO1 inhibition because they have an intact genome with minimal or no DNA damage. The figure below depicts the process by which SINE compounds inhibit the XPO1 nuclear export of tumor suppressor proteins.

Transient XPO1 Inhibition by SINE Compounds

We believe that the XPO1-inhibiting SINE compounds that we have discovered and developed to date, including Selinexor, have the potential to provide a novel targeted therapy that enable tumor suppressor proteins to remain in the nucleus and promote apoptosis of cancer cells. Moreover, our SINE compounds spare normal cells, which, unlike cancer cells, do not have significant damage to their genetic material, and we believe this selectivity for cancer cells minimizes side effects. We believe that the oral administration of Selinexor and the lack of cumulative or major organ toxicities observed to date in patients treated with Selinexor in our Phase 1 clinical trials create the potential for its broad use across many cancer types, including both hematological and solid tumor malignancies. We believe

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that no currently approved cancer treatments or current clinical-stage cancer drug candidates are selectively targeting the restoration and increase in the levels of multiple tumor suppressor proteins in the nucleus.

In addition to cancer, we believe that our SINE compounds have the potential to provide therapeutic benefit in a number of additional indications, including autoimmune and inflammatory diseases, wound healing, HIV and influenza. We have discovered and are developing a pipeline of SINE compounds that have shown evidence of activity in preclinical models of inflammation, wound healing and viral infection. Specifically, our SINE compounds have shown potent evidence of anti-inflammatory activity in several animal models of inflammation, including systemic lupus erythematosus, multiple sclerosis and rheumatoid arthritis. Our SINE compounds have also shown evidence of activity as topical formulations in wound healing by accelerating wound closure and improving wound appearance in both mouse and pig models of surgical and/or knife wounds. In addition, in preclinical studies, our SINE compounds have shown evidence of activity against specific viruses which require XPO1 for their replication, including HIV and influenza.

Our Initial Indication: Cancer

Cancer is a leading cause of death worldwide, with approximately 580,000 people in the United States and 7.6 million people in the world projected to die of cancer in 2014 according to the American Cancer Society. The American Cancer Society also projects that approximately 1.7 million new cancer cases will be diagnosed in the United States in 2014. The International Agency for Research on Cancer projects that, by 2030, 20 million to 26 million people will be diagnosed with cancer, and 13 million to 17 million will die of cancer, each year worldwide.

The most common methods of treating patients with cancer are surgery, radiation and drug therapy. A cancer patient often receives treatment with a combination of these methods. Surgery and radiation therapy are particularly effective in patients in whom the disease is localized. Physicians generally use systemic drug therapies in situations in which the cancer has spread beyond the primary site or cannot otherwise be treated through surgery. In many cases, drug therapy entails the administration of several different drugs in combination. An early approach to cancer treatment was to develop drugs, referred to as cytotoxic drugs, that kill rapidly proliferating cancer cells through non-specific mechanisms, such as disrupting cell metabolism or causing damage to cellular components required for survival and rapid growth. While these drugs have been effective in the treatment of some cancers, they act in an indiscriminate manner, killing healthy cells, as well as cancer cells. Due to their mechanism of action, many cytotoxic drugs have a narrow dose range above which the toxicity causes unacceptable or even fatal levels of damage and below which the drugs are not effective in promoting cancer cell death. A different approach to pharmacological cancer treatment has been to develop drugs, referred to as targeted therapeutics, that target specific biological molecules in the human body that play a role in rapid cell growth and the spread of cancer. Targeted therapeutics are designed to specifically enable the death of cancer cells and spare normal cells, to improve efficacy, and to minimize side effects. The drugs are designed to either attack a target that causes uncontrolled growth of cancer cells because of either a specific genetic alteration primarily found in cancer cells, but not in normal cells, or a target that cancer cells are more dependent on for their growth in comparison to normal cells.

Our SINE approach is a novel targeted therapeutic approach specifically focused on selectively targeting the restoration and increase in the levels of multiple tumor suppressor proteins and growth regulatory proteins in the nucleus. Unlike many other targeted therapeutic approaches which only work for a specific set of cancers or in a specific sub-group of patients, we believe there is evidence to suggest that our SINE compounds have the potential to provide therapeutic benefits across a broad range of both hematological and solid tumor malignancies and benefit a wide range of patients.

Table of Contents**Our Drug Candidates*****Our Lead Drug Candidate Selinexor (KPT-330)****Overview*

Our lead drug candidate, Selinexor (KPT-330), is a wholly-owned, orally available, small molecule, potent SINE compound that specifically blocks XPO1 cargo binding. Selinexor inhibits the export of tumor suppressor proteins out of the nucleus. As a result, these proteins are retained in the nucleus where they can detect cancerous changes and promote the death of cancer cells. We are currently conducting three open-label Phase 1 clinical trials of Selinexor, the first in patients with heavily pretreated relapsed and/or refractory hematological malignancies, the second in patients with heavily pretreated relapsed and/or refractory solid tumor malignancies, and the third, a food effect study, in patients with metastatic, locally advanced or locally recurrent soft tissue or bone sarcomas. We have observed preliminary evidence of anti-cancer activity of Selinexor across a spectrum of patients with advanced cancers who had received multiple previous treatments and, despite these treatments, had disease that was progressing at the time of enrollment in our clinical trials. We believe that the oral administration of Selinexor and lack of cumulative or major organ toxicities observed to date in patients treated with Selinexor in our ongoing Phase 1 clinical trials create the potential for its broad use across many cancer types. Assuming continued positive results from our ongoing Phase 1 and Phase 2 clinical trials of Selinexor and pending regulatory feedback, we plan to initiate registration-directed clinical trials of Selinexor in three hematological malignancy indications during 2014. We expect to initiate these clinical trials for Selinexor in AML, DLBCL and Richter's Syndrome. We plan to seek regulatory approvals of Selinexor in North America and Europe in each such indication with respect to which we receive positive clinical trial results and positive regulatory feedback. We may seek such approvals in other geographies as well. In solid tumor malignancies, we have initiated Phase 2 clinical trials of Selinexor in relapsed glioblastoma multiforme and in ovarian, cervical and uterine carcinomas and expect to initiate Phase 2 clinical trials in squamous head, neck or lung cancers and hormone and chemotherapy refractory metastatic prostate cancer during 2014. We intend to enter into collaborations for marketing and commercialization of Selinexor in particular geographies at an appropriate time.

In May 2012, we filed two investigational new drug applications, or INDs, with the U.S. Food and Drug Administration, one covering Selinexor in advanced hematological malignancies and the other covering Selinexor in advanced or metastatic solid tumor malignancies. The trials in patients with these two indications were initiated in mid-2012 and are being conducted at cancer centers in the United States, Canada and Denmark. In July 2013, we began enrollment in our third Phase 1 clinical trial of Selinexor, a food effect study that is being conducted in the United States and Canada. We are also gathering additional safety and efficacy data regarding Selinexor as part of the food effect study. To date, over 240 patients have received Selinexor in these three clinical trials.

Advanced Hematological Malignancies

Our Phase 1 clinical trial of Selinexor in patients with advanced hematological malignancies continues to enroll patients with documented progressive disease at the time of enrollment. These patients have relapsed and/or refractory hematological malignancies, meaning that their cancers are no longer responsive, or were never responsive, to treatment with approved and/or experimental therapies. These patients had received multiple previous treatments, which we refer to as heavily pretreated.

There are six arms to this clinical trial:

Arm 1 includes patients with the following chronic B-cell malignancies: multiple myeloma, or MM, Waldenström's Macroglobulinemia, or WM, chronic lymphocytic leukemia, or CLL, Richter's Syndrome, or RS, and Non-Hodgkin's Lymphoma, or NHL, including NHL that

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has transformed from slowly growing, or indolent, to aggressive, or Transformed NHL, DLBCL, mantle cell lymphoma, or MCL, and follicular lymphoma, or FL.

Arm 2 includes patients with AML of any subtype except one specified subtype known as M4.

Arm 3 includes patients with T-cell lymphomas.

Arm 4 includes patients with chronic myeloid leukemia, or CML.

Arm 5 includes patients with acute lymphocytic leukemia, or ALL.

Arm 6 includes patients with MM or WM taking 20 mg/m² of dexamethasone with each dose of Selinexor.

We designed this open-label Phase 1 clinical trial to evaluate the safety of Selinexor, to determine the Phase 2 clinical trial dose and dosing schedule and to evaluate preliminary anti-cancer activity of Selinexor. Currently, Selinexor is orally administered twice per week over a 28-day cycle at up to 80 mg/m². We expect to treat up to approximately 250 patients over the course of this clinical trial, with approximately 125 patients expected to be evaluated in Arm 1 and approximately 75 patients expected to be evaluated in Arm 2. We expect to treat up to approximately 12, eight, six and 20 patients in Arms 3, 4, 5 and 6, respectively.

Arm 1. As of December 4, 2013, a total of 60 patients on Arm 1 (26 with MM, three with WM, 23 with NHL, four with CLL and four with RS) have been enrolled at doses ranging from 3 mg/m² to 45 mg/m² at eight clinical centers in the United States, Canada and Denmark. We have observed preliminary evidence of anti-cancer activity in certain of these heavily pretreated patients. Potential responses include CR, which for CLL means complete remission and for the other indications listed means complete response, PR, which for CLL means partial remission and for the other indications listed means partial response, MR, which means minimal response for all indications listed and SD, which means stable disease for all indications listed, each as determined in accordance with commonly accepted evaluation criteria for the specific indication. 45 of the 55 patients (82%) evaluated as of December 4, 2013 in this arm have experienced PR, MR or SD. The distribution of these responses across indications as of December 4, 2013 was as follows: a partial response or partial remission in nine patients, one in each of MM, RS, MCL and FL, two in CLL and three in DLBCL; a minimal response in seven patients, four in MM and three in WM; and stable disease in 29 patients, 15 in MM, five in DLBCL, one in MCL, four in FL, two in CLL and two in RS. Eight of the 55 patients (15%) evaluated as of December 4, 2013 in this arm have experienced PD, including four patients with MM, two patients with DLBCL and two patients with transformed NHL. As of December 4, 2013, five patients either had not yet been evaluated or were deemed non-evaluable, meaning the patient's response could not be evaluated due to a number of potential factors, including when a patient withdraws consent or fails to comply with therapeutic protocol for the trial.

Responses are shown in the table below for the 55 patients who had been evaluated as of December 4, 2013, each of whom received a dose between 3 mg/m² to 45 mg/m² per cycle. As of December 4, 2013, patients receiving a dose higher than 45 mg/m² had not yet been evaluated. These responses are interim unaudited data based on site reports and are measured using commonly accepted evaluation criteria for the specific indication.

Table of Contents**Responses in Arm 1 (Chronic B-Cell Malignancies) [3 mg/m² to 45 mg/m²] as of December 4, 2013**

Cancer	Number of Patients Evaluated	Total PRs, MRs and SDs					
		SD (%)	PR (%)	MR (%)	SD (%)	PD (%)	WC (%)
MM	25	20 (80%)	1 (4%)	4 (16%)	15 (60%)	4 (16%)	1 (4%)
WM	3	3 (100%)		3 (100%)			
CLL	4	4 (100%)	2* (50%)		2 (50%)		
RS	3 [#]	3 (100%)	1 (33%)		2 (67%)		
NHL							
DLBCL	10	8 (80%)	3 (30%)		5 (50%)	2 (20%)	
MCL	2	2 (100%)	1 (50%)		1 (50%)		
FL	6	5 (83%)	1 (17%)		4 (67%)		1 (17%)
Transformed	2					2 (100%)	
Total	55 (100%)	45 (82%)	9 (16%)	7 (13%)	29 (53%)	8 (15%)	2 (4%)

*

These PRs in CLL patients refer to lymph node response only.

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We previously reported that four patients with Richter's Syndrome were evaluated as of December 4, 2013. One of these four patients was subsequently deemed non-evaluable as of December 4, 2013 and is not included in the response data presented here.

PD means progressive disease, as determined in accordance with commonly accepted evaluation criteria for the specific indication. Withdrew consent, or WC, means a patient withdrew from the trial before evaluation. Patients who have not yet been evaluated or are considered non-evaluable are not included in the response data.

Enrollment in this arm began in July 2012. In order to remain on study, patients must exhibit a response of SD or better at each evaluation, which typically occurs at the end of each 28-day dosing cycle. A response of SD represents a stabilization of the disease, as determined in accordance with commonly accepted evaluation criteria for the specific indication, over one dosing cycle, which we believe is an indicator of the anti-cancer effect of the drug candidate. As of December 4, 2013, fifteen patients in this arm remained on study. As of December 4, 2013, five patients had remained on study in this arm for longer than nine months, including three patients who had been on study for longer than twelve months and one patient who had been on study for longer than 15 months. Three of the five patients continued to remain on study as of December 4, 2013. No major organ toxicities have been observed in this arm to date.

The most common side effects in this arm, known as adverse events, or AEs, are Grade 1 or Grade 2 adverse events. Grade 1 and 2 adverse events are generally characterized as mild. Grade 3 adverse events are considered moderate and Grade 4 adverse events are considered severe. As of December 4, 2013, we have reports of AEs in 55 of the 60 patients enrolled in this arm and the AE prevalence percentages below are based upon the 59 patients from whom we have collected safety data as of December 4, 2013. Gastrointestinal adverse events and fatigue are the most common types of adverse events seen in Arm 1. As of December 4, 2013, the gastrointestinal events typically consist of nausea in 41 patients (69%), anorexia in 31 patients (53%), vomiting in 20 patients (34%) and diarrhea in 18 patients (31%). The gastrointestinal events are solely either Grade 1 or Grade 2 events and are generally responsive to standard supportive care. Grade 1 or Grade 2 fatigue was observed in 30 patients (51%) in this arm as of December 4, 2013, with three additional patients (5%) showing Grade 3 fatigue. We have also observed Grade 3 or Grade 4 thrombocytopenia, or low count of platelets in the blood, in 14 patients (24%), with four additional patients (7%) showing Grade 1 or Grade 2 thrombocytopenia. We have also observed Grade 3 or Grade 4 neutropenia, or low neutrophil counts, in 13 patients (22%), with four

additional patients (7%) showing Grade 1 or Grade 2 neutropenia. We

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expect that thrombocytopenia and neutropenia are primarily a result of patients entering this arm with marked bone marrow suppression due to both disease and prior therapies. We do not gather data regarding the number of patients that have withdrawn from this arm as a result of AEs.

Due to the gastrointestinal events we observed earlier in the arm, we now instruct physicians to initiate supportive care and medications prior to patients beginning on Selinexor therapy. The supportive care consists primarily of focusing on maintaining caloric and fluid intake as well as the introduction of appetite stimulants and anti-nausea medication. We have seen fewer and milder gastrointestinal events and reduced fatigue as a result of the initiation of supportive care and medications prior to beginning Selinexor therapy.

As of December 4, 2013, there have been 51 serious adverse events, or SAEs, reported in 23 patients in Arm 1. SAEs generally refer to AEs that result in death, are life threatening, require hospitalization or prolonging of hospitalization, or cause a significant and permanent disruption of normal life functions, congenital anomalies or birth defects, or require intervention to prevent such an outcome. SAEs may be attributed to Selinexor or deemed unrelated. Of the 51 SAEs reported as of December 4, 2013, one SAE was deemed by us and the clinical investigator to be related to Selinexor. This SAE was Grade 2 blurred vision. This was not permanent and the patient recovered from this SAE. All patients in this arm at the time received eye examinations by an ophthalmologist and all new patients receive the same examination prior to beginning treatment in order to assess any changes in vision while on Selinexor therapy.

No dose limiting toxicities, or DLTs, were observed at the 30 mg/m² or above dose levels in Arm 1. We are continuing with dose escalation and fixed dose expansion cohorts in Arm 1.

Arm 2. As of December 4, 2013, a total of 39 patients with heavily pretreated relapsed and/or refractory AML were enrolled in this arm and the majority of these patients are elderly, meaning 60 years of age or older. We have observed preliminary evidence of anti-cancer activity in certain of the patients in this arm. Potential responses include CR, which for AML means complete remission with complete blood count recovery, CR(i), which for AML means complete remission with incomplete blood count recovery, PR, which for AML means partial remission, MLFS, or morphologic leukemia-free state and SD. Seventeen of the 33 patients (52%) evaluated as of December 4, 2013 in this arm have experienced a CR, CR(i), PR, MLFS or SD. Five patients experienced CR or CR(i), with four patients experiencing CR and one patient experiencing CR(i), two patients have experienced PR, one patient has experienced MLFS and nine patients have experienced SD. Twelve of the 33 patients (36%) evaluated as of December 4, 2013 in this arm have experienced PD. Six patients had not yet been evaluated or were non-evaluable as of December 4, 2013.

Responses are shown in the table below for the 33 patients who had been evaluated as of December 4, 2013, each of whom received a dose between 16.8 mg/m² to 55 mg/m² per cycle. These responses are interim unaudited data based on site reports and are measured using commonly accepted evaluation criteria for AML.

Responses in Arm 2 (AML) [16.8 mg/m² to 55 mg/m²] as of December 4, 2013

Number of Patients Evaluated	Total CRs, CR(i)s, PRs, MLFS and	CR (%)	CR(i) (%)	PR (%)	MLFS (%)	SD (%)	PD (%)	WC (%)
	SD (%)							
33	17 (52%)	4 (12%)	1 (3%)	2 (6%)	1 (3%)	9 (27%)	12 (36%)	4 (12%)

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Enrollment in this arm began in January 2013. In order to remain on study, patients must exhibit a response of SD or better at each evaluation, which typically occurs at the end of each 28-day dosing cycle. A response of SD represents a stabilization of the disease, as determined in accordance with commonly accepted evaluation criteria for AML, over one dosing cycle, which we believe is an indicator of the anti-cancer effect of the drug candidate. As of December 4, 2013, five patients in this arm remained on study. As of December 4, 2013, five patients had remained on study in this arm for more than three months. Two of these patients continued to remain on study as of December 4, 2013. No major organ toxicities have been observed in this arm to date.

Gastrointestinal adverse events and fatigue are the most common types of AEs seen in Arm 2. As of December 4, 2013, we have reports of AEs in 36 of the 39 patients enrolled in this arm and the AE prevalence percentages below are based upon 38 patients from whom we have collected safety data as of December 4, 2013. As of December 4, 2013, the gastrointestinal adverse events typically consist of nausea in 22 patients (58%), anorexia in 17 patients (45%), vomiting in 13 patients (34%), diarrhea in 12 patients (32%) and weight loss in 10 patients (26%). The gastrointestinal events are primarily Grade 1 or Grade 2 events (95%) that are generally responsive to standard supportive care. Fatigue was observed in 18 patients in this arm (47%) as of December 4, 2013, including Grade 3 fatigue in 3 patients (8%) and Grade 1 or Grade 2 fatigue in 15 patients (40%). We have also observed Grade 4 thrombocytopenia in 3 patients (8%) in this arm as of December 4, 2013. We expect that the thrombocytopenia is primarily a result of patients entering this arm with marked bone marrow suppression due to both disease and prior therapies. We do not gather data regarding the number of patients that have withdrawn from this arm as a result of AEs.

As in Arm 1, we have seen fewer and milder gastrointestinal events and reduced fatigue as a result of the initiation of supportive care and medications prior to beginning Selinexor therapy.

As of December 4, 2013, there have been 54 SAEs reported in 25 patients in Arm 2. Of the 54 SAEs reported, one SAE was deemed by us and the clinical investigator to be related to Selinexor. This SAE was the worsening of a patient's existing cataracts. We do not have data with respect to the status of this SAE.

As of December 4, 2013, no DLTs have been observed in this arm.

Arm 3. We are evaluating Selinexor in patients with heavily pretreated relapsed and/or refractory T-cell lymphoma in Arm 3 of this clinical trial. We began enrollment in August 2013 and have administered Selinexor to one patient in Arm 3 who was non-evaluable as of December 4, 2013.

Arms 4 - 6. As of December 4, 2013, we have not evaluated any patients in these arms of our Phase 1 clinical trial in hematological malignancies. We expect to treat approximately eight patients in Arm 4, six patients in Arm 5 and 20 patients in Arm 6.

Advanced or Metastatic Solid Tumor Malignancies

Our Phase 1 clinical trial of Selinexor in patients with advanced or metastatic solid tumor malignancies continues to enroll patients with documented progressive disease at the time of enrollment. These patients have heavily pretreated relapsed and/or refractory solid tumor malignancies. We have treated patients diagnosed with colorectal cancer, or CRC, squamous cell cancer of the head and neck or lung, ovarian cancer, cervical cancer, endometrial stromal sarcoma, or ESS, melanoma, glioblastoma, or GBM, pancreatic cancer, prostate cancer and other solid tumor malignancies. We designed this open-label Phase 1 clinical trial to evaluate the safety of Selinexor, to determine the Phase 2 clinical trial dose and dosing schedule and to evaluate preliminary anti-cancer activity of Selinexor. Selinexor is orally administered in escalating dose levels two times per week over each 28-day cycle. We expect to treat up to approximately 90 patients over the course of the initial dose

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escalation phase of this clinical trial. We expect to evaluate approximately 74 additional patients in fixed dose expansion cohorts of this trial at the expected Phase 2 clinical trial dose.

As of December 24, 2013, a total of 112 patients have been enrolled at six clinical centers in the United States, Canada and Denmark, and are being treated at doses ranging from 3 mg/m² to 65 mg/m². We have observed preliminary evidence of anti-cancer activity in certain of the patients in this trial. Potential responses include CR, PR and SD, each as determined in accordance with Response Evaluation Criteria In Solid Tumors, or RECIST, the commonly accepted evaluation criteria for solid tumor malignancies. Forty-five of the 94 patients (48%) evaluated as of December 24, 2013 in this trial have experienced a PR or SD, including a PR in three patients; 42 patients have experienced SD. Forty-nine of the 94 patients (52%) evaluated as of December 24, 2013 in this trial have experienced PD. Eighteen patients had not yet been evaluated or were non-evaluable as of December 24, 2013.

Responses are shown in the table below for the 94 patients who had been evaluated as of December 24, 2013, each of whom received a dose between 3 mg/m² to 65 mg/m² per cycle. These responses are interim unaudited data based on site reports and are evaluated in accordance with RECIST.

Responses in Advanced or Metastatic Solid Tumor Malignancies [3 mg/m² to 65 mg/m²] as of December 24, 2013

Cancer	Number of Patients Evaluated	Total PRs and			
		SD (%)	PR (%)	SD (%)	PD (%)
CRC	35	13 (37%)	1 (3%)	12 (34%)	22 (63%)
Head & Neck	13	9 (69%)		9 (69%)	4 (31%)
Lung	5	3 (60%)		3 (60%)	2 (40%)
Ovarian	5	3 (60%)	1 (20%)	2 (40%)	2 (40%)
Cervical	4	2 (50%)		2 (50%)	2 (50%)
Endometrial Stromal Sarcoma	6	5 (83%)		5 (83%)	1 (17%)
Melanoma	3	2 (67%)	1 (33%)	1 (33%)	1 (33%)
Pancreas	4				4 (100%)
Prostate	5	5 (100%)		5 (100%)	
Other	9	3 (33%)		3 (33%)	6 (67%)
GBM	5				5 (100%)
Total	94 (100%)	45 (48%)	3 (3%)	42 (45%)	49 (52%)

Enrollment in this trial began in June 2012. In order to remain on study, patients must exhibit a response of SD or better at each evaluation, which typically occurs following the completion of two 28-day dosing cycles. A response of SD represents a stabilization of the disease, as determined in accordance with RECIST, over one dosing cycle, which we believe is an indicator of the anti-cancer effect of the drug candidate. As of December 24, 2013, 26 patients in this clinical trial remained on study. As of December 24, 2013, 11 patients had remained on study for more than six months, including two patients on study for longer than eight months, and one patient had remained on study for longer than 17 months. Five of the 11 patients on study for more than six months remained on study as of December 24, 2013. No major organ toxicities have been observed in this trial to date.

The most common AEs associated with Selinexor in patients with advanced or metastatic solid tumor malignancies are gastrointestinal in nature or fatigue. As of December 24, 2013, we have reports of AEs in 106 of the 112 patients enrolled in this arm and the AE prevalence percentages below are based upon 112 patients from whom we have collected safety data as of December 4, 2013. As of December 24, 2013, the gastrointestinal adverse events typically consist of nausea in 74 patients (66%), anorexia in 66 patients (59%), vomiting in 54 patients (48%), dysgeusia, or a distortion in the sense of

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taste, in 35 patients (31%), weight loss in 37 patients (33%) and diarrhea in 30 patients (27%). The gastrointestinal events are primarily Grade 1 or Grade 2 events (94%) that are generally responsive to standard supportive care. Fatigue was observed in 83 patients (74%) as of December 24, 2013, including Grade 3 fatigue in 16 patients (14%) and Grade 1 or Grade 2 fatigue in 67 patients (60%). Anemia, or a decrease in red blood cell count, was observed in 30 patients (27%) as of December 24, 2013, including Grade 3 anemia in 8 patients (7%) and Grade 1 or Grade 2 anemia in 22 patients (20%). As of December 24, 2013, seven patients have withdrawn from this trial as a result of AEs.

As in our hematological malignancy clinical trial, we have seen fewer and milder gastrointestinal events and reduced fatigue as a result of the initiation of supportive care and medications prior to beginning Selinexor therapy.

As of December 24, 2013, there have been 89 SAEs reported in 43 patients in this clinical trial. Of the 89 SAEs reported, three were deemed by us and the applicable clinical investigator to be related to Selinexor. One of these SAEs was dehydration and the other two were the development or worsening of cataracts. These SAEs were not permanent and the patients recovered following supportive care.

As of December 24, 2013, no DLTs were observed in the initial six cohorts at doses ranging from 3 to 30 mg/m². Of the three patients who received 10 doses per cycle at 40 mg/m², there were two DLTs. One was Grade 3 anorexia with dehydration and fatigue, and the other was Grade 3 fatigue with Grade 1-2 anorexia. Although we believe that neither of these patients with DLTs received optimal supportive care, given the overall clinical picture, we made the decision to establish 10 doses per cycle at 30 mg/m² to be the maximum tolerated dose for advanced or metastatic solid tumor malignancy patients. As a result of our decision regarding the maximum tolerated dose, the dose of a third patient being treated at 40 mg/m², who had tolerated therapy well, was also reduced to 30 mg/m². We have also evaluated 10 additional patients at 10 doses per cycle at 30 mg/m² and no DLTs were observed.

We are evaluating a dosing schedule of eight doses per cycle. At eight doses per cycle, a maximum tolerated dose has not yet been established and no DLTs have been observed. Currently, a dose of 85 mg/m² at eight doses per cycle is being evaluated in patients with solid tumor malignancies. We are continuing with dose escalation and fixed dose expansion cohorts in this clinical trial.

Metastatic, Locally Advanced or Locally Recurrent Soft Tissue or Bone Sarcomas (Food Effect Study)

In July 2013, we began enrollment in our third clinical trial of Selinexor, a Phase 1b open-label food effect study in heavily pretreated patients who have metastatic, locally advanced or locally recurrent soft tissue or bone sarcomas. The trial is primarily designed to evaluate the effects of food and formulation (capsules and tablets) on the absorption of oral Selinexor. We are also gathering additional safety and efficacy data regarding Selinexor in this trial. We are currently using the capsule formulation in our other Phase 1 clinical trials. As of December 24, 2013, 19 patients have been enrolled in this clinical trial and sixteen were evaluable for response. We plan to enroll up to approximately 20 patients in this study in the United States and Canada. In light of the results that we have seen in this trial to date, we believe that the new tablet formulations of Selinexor have similar pharmacokinetics and tolerability as the original capsule formulations that are used in our Phase 1 studies. We have also confirmed that Selinexor is better absorbed when taken with food. We expect to use the tablet formulation in our registration-directed clinical trials for Selinexor in hematological indications and our Phase 2 clinical trials for Selinexor in solid tumor malignancies.

Clinical Development Plan

We have observed preliminary evidence of anti-cancer activity of Selinexor across a spectrum of patients with heavily pretreated relapsed and/or refractory cancers. Furthermore, several patients have remained on Selinexor for greater than eight months, and in some cases, over one year. We believe

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that the fact that patients have remained on Selinexor for such periods of time indicates that Selinexor has the potential to treat certain relapsed and/or refractory cancers. In addition, because the AEs and SAEs observed to date in our Phase 1 clinical trials have generally been lower grades and have been mitigated by supportive care, we believe Selinexor is sufficiently well-tolerated to allow patients to remain on therapy for prolonged periods. Assuming continued positive results from our ongoing Phase 1 and Phase 2 clinical trials of Selinexor and pending regulatory feedback, we plan to initiate registration-directed clinical trials of Selinexor in three hematological malignancy indications during 2014. We expect to initiate these clinical trials for Selinexor in AML, DLBCL and Richter's Syndrome. We plan to seek regulatory approvals of Selinexor in North America and Europe in each such indication with respect to which we receive positive clinical trial results and positive regulatory feedback. We may seek such approvals in other geographies as well. In solid tumor malignancies, we have initiated Phase 2 clinical trials of Selinexor in relapsed glioblastoma multiforme and in ovarian, cervical and uterine carcinomas and expect to initiate Phase 2 clinical trials in squamous head, neck or lung cancers and hormone and chemotherapy refractory metastatic prostate cancer during 2014.

Acute Myeloid Leukemia in Elderly Patients

Acute myeloid leukemia, or AML, in elderly populations remains a vexing clinical problem. AML is a cancer that starts in the bone marrow and in most cases quickly moves into the blood. The incidence of AML dramatically increases after the age of 55. The American Cancer Society estimates that approximately 18,860 new cases of AML, most of which will be in adults, will be diagnosed in the United States in 2014. Given the shift in demographics in the population in the Western hemisphere, it is likely that an increased number of elderly individuals will be diagnosed with this form of cancer. Aside from a general increase in the incidence of AML in the general population, three additional patient populations are contributing to the increasing number of AML cases: an increasing number of older persons are developing a disease called myelodysplastic syndrome, or MDS, which can convert to AML; certain types of chemotherapy, such as alkylating agents used to treat Hodgkin's disease, breast cancer, and other disorders, can increase the risk of developing AML later in life; and patients with chronic myelogenous leukemia treated long term with imatinib (Gleevec) and other drugs can have their disease reach an accelerated or blast phase, converting to AML.

About 40% of AML patients are young enough and fit enough to undergo bone marrow transplantation for their AML, and about 50% of these patients can be cured of their disease. Those that are not cured, and patients who are elderly or unfit for transplant, have a very poor prognosis. The median survival for elderly patients with AML is less than a year and worsens continuously with advancing age to as low as one month for those who are older than 85 years of age. The obstacles to effective therapy in older patients include their heightened susceptibility to drug-related toxicity, which is often due to co-existing medical problems and/or poor organ function, and their lower response to chemotherapy. In addition, the poorer response to therapies in elderly AML patients is due to a higher frequency of high-risk cytogenetic lesions, a type of DNA mutation, compared with their younger counterparts with AML. Even for those elderly patients able to tolerate chemotherapy, complete remission rates are well less than half the complete remission rates for younger adults: about 25 percent in patients older than 70 years old compared to 70 percent in patients younger than 50 years old. In addition, the cases of elderly AML that arise from MDS, or the ineffective production of the myeloid class of blood cells, mean that there are few normal stem cells for those patients available for hematologic recovery after chemotherapy. As a result, complications, hospitalizations and deaths from cytopenias, or reductions in the number of certain blood cells, are common among the elderly with AML.

Over the past two decades, many compounds have been evaluated in elderly patients with AML, but due to significant toxicities and/or lack of efficacy, none has been approved to date. Preclinical data on our SINE compounds from several groups at Dana-Farber Cancer Institute, Ohio

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State University and MD Anderson Cancer Center have shown preliminary evidence of anti-cancer activity of our SINE compounds against a set of AML cell lines with diverse genetics, as well as against leukemia stem (initiating) cells. In addition, in our Phase 1 clinical trial of Selinexor in patients with advanced hematological malignancies, as described above, we have observed preliminary evidence of anti-cancer activity of Selinexor in elderly patients (those over 60 years of age) with heavily pretreated relapsed and/or refractory AML. We have observed CRs, CR(i)s, PRs, MLFS or SD in 48% of these patients as of December 4, 2013 and, in many cases, the response has been maintained for longer than two months. We believe that these initial results suggest that Selinexor has the potential to demonstrate anti-cancer activity and tolerability in elderly patients with heavily pretreated AML.

Based on the results observed to date in our Phase 1 clinical trial of Selinexor in patients with advanced hematological malignancies and the expansion cohort in Arm 2 of this trial consisting primarily of elderly patients with AML, we expect to initiate a randomized, registration-directed Phase 2 clinical trial of Selinexor in patients over 60 years of age with AML in first relapse who are not candidates for intensive chemotherapy or transplantation. The Phase 2 trial is expected to enroll about 150 patients who will be randomized so that for every three patients, two receive Selinexor and one receives the treating physician's choice. The physician's choice includes best supportive care, or BSC, which includes transfusions, antibiotics and growth factors as appropriate, or BSC with low dose Ara-C, or BSC with a hypomethylating agent such as azacytidine or decitabine. There are currently no approved agents for these patients, and there are no generally recognized standards of care in this population. The primary endpoint is overall survival. Selinexor will be given at a dose of 55 mg/m², administered orally twice per week. The trial is expected to begin in the first half of this year and is expected to take two years to complete.

Diffuse Large B-Cell Lymphoma

NHL is a cancer that starts in cells called lymphocytes, which are part of the body's immune system. Lymphocytes are found in the lymph nodes and other lymphoid tissues (such as the spleen and bone marrow). According to the American Cancer Society, about 70,800 patients will be diagnosed with NHL in the United States in 2014. Diffuse large B-cell lymphoma, or DLBCL, is the most common of the aggressive NHLs, accounting for about one out of every three newly-diagnosed cases of NHL in the United States, according to the American Cancer Society. According to the Leukemia and Lymphoma Society, NHL rates, including DLBCL, have steadily increased 3 to 4% each year in the United States from 1973 to the mid-1990s.

These increases in NHL rates have been observed across all major demographic groups (except for the very young), without a clear cause. Such temporal increases in incidence of a particular form of cancer are atypical. Improved cancer reporting, more sensitive diagnostic techniques, particularly for borderline lesions, changes in classification of lymphoproliferative diseases, which are diseases where lymphocytes are produced in excessive quantities, and, in particular, the increasing occurrence of AIDS-associated DLBCL, have contributed to the escalation of incidence of this disease. Non-AIDS related NHL incidence rates have continued to increase, specifically the rates among females, older males and blacks. For the vast majority of patients, the etiology of DLBCL is unknown.

The fundamental treatment of DLBCL has changed little in the past two decades, with no new or targeted agents approved for this indication. Initial therapy with multiagent, or three to four, cytotoxic drugs in combination with the monoclonal antibody rituximab (Rituxan®) leads to responses in greater than 75% of patients. In patients who are less than 65 years old, and who have good organ function, high dose chemotherapy with stem cell transplantation can lead to cures in approximately 50% of these patients. Older patients relapsing after initial chemotherapy, and those relapsing after stem cell transplantation, have a very poor prognosis, and the expected survival of such patients is less than one year. Newer targeted agents such as the BTK inhibitor ibrutinib and the immunomodulatory drug lenalidomide (Revlimid®) have shown activity in the immunoblastic (activated B cell) type of

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DLBCL in clinical trials, but responses are generally short-lived. Responses are much lower in the germinal center, or GC, type of DLBCL. Therefore, we believe that novel, well-tolerated drugs are needed for the treatment of relapsed DLBCL, particularly because ibrutinib and Revlimid have not been approved by the FDA for the treatment of DLBCL.

In our Phase 1 clinical trial of Selinexor in patients with advanced hematological malignancies, Selinexor has shown preliminary evidence of anti-cancer activity in patients with DLBCL. As of December 4, 2013, eight out of 10 patients (80%) evaluated with DLBCL have responded to treatment and the response has been maintained in four of these eight patients (50%) for longer than two months. Based on the results observed to date in this Phase 1 clinical trial, we expect to initiate a randomized, registration-directed clinical trial for Selinexor in DLBCL in late summer 2014. This trial is expected to enroll approximately 300 DLBCL patients who have progressed after at least two lines of chemotherapy and anti-CD20 monoclonal antibodies. This trial will be randomized so that for every three patients, two receive Selinexor and one receives the treating physician's choice of chemotherapy. The primary endpoint is progression free survival. Selinexor will be given at a dose of 60 mg/m², administered orally twice per week.

Richter's Syndrome

Richter's Syndrome (also called Richter's Transformation) describes the transformation from chronic lymphocytic leukemia, or CLL, to DLBCL, a type of NHL. The American Cancer Society estimates that 15,720 patients will be diagnosed with CLL in the United States in 2014. Approximately 5% to 10% of patients with CLL will experience Richter's Syndrome, which is characterized by a distinct worsening of symptoms. Although there are no specific therapies approved to treat Richter's Syndrome, multi-agent chemoimmunotherapy is typically used as a first line treatment.

In our Phase 1 clinical trial of Selinexor in patients with advanced hematological malignancies, Selinexor has shown preliminary evidence of anti-cancer activity in patients with Richter's Syndrome. As of December 4, 2013, three out of three patients (100%) evaluated with Richter's Syndrome have responded to treatment. Based on the results observed to date in this Phase 1 clinical trial, we are also planning to initiate a registration-directed, single arm clinical trial in the middle of 2014 that is expected to enroll approximately 50 patients with Richter's Syndrome whose disease has relapsed after initial treatment, which is typically multi-agent chemoimmunotherapy. This clinical trial will not be randomized as there are no generally accepted second-line treatments for Richter's Syndrome and, therefore, no available therapies to serve as a control arm for the trial. Consequently, the primary endpoint is overall response rate. Selinexor will be administered orally twice per week at a dose that has not yet been determined.

Multiple Myeloma

Multiple myeloma, or MM, is a hematological malignancy characterized by the accumulation of monoclonal plasma cells in the bone marrow, the presence of monoclonal immunoglobulin, or M protein, in the serum or urine, bone disease, kidney disease, and immunodeficiency. It is more common in elderly patients, with a median age at diagnosis of 65-70 years. In the United States, the American Cancer Society estimates that there will be approximately 24,050 new cases of MM in 2014. M protein, produced by most MM tumors, has been an established biomarker of the disease and the extent of the disease for over 30 years. More recently, the measurement of a fragment of the M protein, the free light chain, has been used as an additional biomarker of the disease and the extent of the disease in a subset of MM patients.

The treatment of MM has improved in the last 20 years due to the use of high-dose chemotherapy and autologous stem cell transplantation, and the subsequent introduction of the immunomodulatory agents thalidomide and lenalidomide and the proteasome inhibitor bortezomib. The

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median overall survival of MM patients, meaning the length of time an MM patient survives with the disease, has increased significantly in patients younger than 50 years old, with those patients experiencing a 10-year survival rate of around 40%, meaning that 40% of those patients are still alive after 10 years. However, despite the increased effectiveness of the first-line agents, the majority of patients will eventually relapse and become drug-resistant. Although a wide variety of new agents are being used in relapsed and/or refractory patients, including new proteasome inhibitors (carfilzomib, ixazomib, oprozomib, and marizomib), immunomodulatory drugs (pomalidomide), monoclonal antibodies (elotuzumab and daratumumab), a signal transduction modulator (perifosine), and histone deacetylase inhibitors (vorinostat and panobinostat), we believe that there remains a need for therapies in these relapsed and/or refractory patients that can improve the overall survival rate.

In our Phase 1 clinical trial of Selinexor in patients with advanced hematological malignancies, Selinexor has shown preliminary evidence of anti-cancer activity in patients with MM. As of December 4, 2013, 25 MM patients had been evaluated in our trial. Twenty of the 25 patients (80%) with progressive MM on entry experienced either a PR, an MR or SD, while four of 25 (16%) had PD. The remaining patient withdrew from the trial. Some of these patients experiencing either a PR, an MR or SD have a form of MM called light chain disease. Patients with light chain MM generally have a prognosis that is worse than patients with usual MM, where the myeloma protein is composed of both light and heavy chains. Light chain MM represents approximately 15% to 20% of MM cases and generally does not respond to therapies as well as the usual MM. Given the preliminary responses of patients with light chain MM observed to date in our Phase 1 clinical trial of Selinexor in patients with advanced hematological malignancies, and the unmet medical need in light chain MM, we may decide to initiate additional clinical trials of Selinexor in light chain MM. If we are able to confirm the preliminary evidence of anti-cancer activity of Selinexor in our expansion cohort of MM patients, including both usual and light chain MM, we may decide to initiate a registration-directed clinical trial in MM.

Solid Tumors and Other Cancer Indications

We have also observed preliminary evidence of anti-cancer activity of Selinexor in our Phase 1 clinical trial of patients with advanced or metastatic solid tumor malignancies. We have initiated Phase 2 clinical trials of Selinexor in relapsed glioblastoma multiforme and in ovarian, cervical and uterine carcinomas and expect to initiate Phase 2 clinical trials in squamous head, neck or lung cancers and hormone and chemotherapy refractory metastatic prostate cancer during 2014.

We also expect a number of investigator sponsored trials, or ISTs, to be initiated in a variety of both hematological and solid tumor malignancies in 2014. These ISTs could consist of single agent or combination studies with other agents in both hematological and solid tumor malignancies.

Preclinical Studies

Selinexor was administered in efficacy studies to mice implanted with human tumors, or xenografts. We observed evidence of anti-cancer activity of Selinexor in mouse models of myeloma, MCL and T-cell acute lymphocytic leukemia xenografts. In addition, we observed anti-cancer activity of Selinexor, including survival advantages in models of orthotopic MM, and in several NHL xenografts, as well as in orthotopic leukemia models of AML, ALL and CLL. We have also observed evidence of anti-cancer activity of Selinexor in solid tumor xenografts including prostate, breast, neuroblastoma, melanoma, lung, glioblastoma, alveolar soft part sarcoma, colon and ovarian cancers. In addition, we performed preclinical studies of Selinexor in combination with paclitaxel, velboraf (B-raf inhibitor), irinotecan, topotecan and radiation therapy. In all of these preclinical studies of Selinexor in combination with other drugs, we observed evidence of additive and/or synergistic effects with inhibition of tumor growth. In addition, we have observed evidence of anti-cancer activity with

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Verdinexor, an oral SINE compound closely-related to Selinexor, in dogs with newly-diagnosed or first relapse after chemotherapy lymphomas.

Our Other Drug Candidates

KPT-350 and Related SINE Compounds

As described above, XPO1 mediates the nuclear export of many different cargo proteins. Several of these proteins play key roles in inflammation and related processes. Nuclear factor κ B, or NF- κ B, is a protein that plays very important roles in many types of inflammation. In cells, NF- κ B can be inhibited by another protein called I κ B, or Inhibitor of NF- κ B, that binds to NF- κ B and prevents NF- κ B from binding to DNA and driving inflammation. When inflammation occurs, XPO1 transports I κ B out of the nucleus into the cytoplasm where it cannot inhibit NF- κ B activity. When KPT-350 or a similar SINE compound inhibits XPO1, I κ B export to the cytoplasm is blocked and I κ B accumulates in the nucleus. The I κ B in the nucleus binds to NF- κ B and blocks its inflammatory activity. KPT-350 or a similar SINE compound also increases the concentration of other inhibitors of NF- κ B in the nucleus such as FOXO and COMMD1 proteins. Thus, XPO1 inhibition leads to potent, multifaceted inhibition of the inflammatory mediator NF- κ B.

KPT-350 and similar SINE compounds have additional important anti-inflammatory activities such as activation of the proteins RXR γ , PPAR γ and NRF2 (an anti-oxidant and neuroprotective protein). Finally, in human patients treated with Selinexor, we observed reductions in the numbers of eosinophils, which are white blood cells that are associated with inflammation and allergies. Our SINE compounds have shown broad evidence of anti-inflammatory activity across preclinical models of the following diverse autoimmune diseases: rheumatoid arthritis, systemic lupus erythematosus, and multiple sclerosis. These observations suggest that SINE compounds have multiple anti-inflammatory effects. We are evaluating several SINE compounds, including KPT-350, in additional inflammatory models and preclinical safety studies.

PAK4 Inhibitors

In addition to our SINE compounds, we also investigate XPO1 cargo proteins and their role in cell cycle and division. As part of this investigation, we have identified several XPO1 cargo proteins whose inhibition leads to the selective death of cancer cells. One of the XPO1 cargo proteins that we identified was P21-activated kinase 4, or PAK4. PAK4 is a signaling protein regulating numerous fundamental cellular processes, including intracellular transport, cellular division, cell shape and motility, cell survival, immune defense and the development of cancer. PAK4 interacts with many key signaling molecules involved in cancer such as beta-catenin, CDC42, Raf-1, BAD and myosin light chain. Based on this biology, we used our drug discovery and optimization platform to identify small molecule inhibitors of PAK4. Our PAK4 inhibitors have shown broad evidence of anti-cancer activity against hematological and solid tumor malignancies cells while showing minimal toxicity to normal cells *in vitro*. In mouse xenograft studies, our PAK4 inhibitors given orally have shown evidence of anti-cancer activity and tolerability. If we confirm these preliminary results in future preclinical studies, we may initiate IND-enabling toxicology studies with one or more PAK4 inhibitors.

Verdinexor (KPT-335)

We have used spontaneously occurring dog cancers as a surrogate model for human malignancies. It is widely known that canine lymphomas respond to chemotherapy similarly to their human counterpart (human NHL) and display a comparable genetic profile. Lymphomas are one of the most common tumors in pet dogs. Lymphoma in dogs is very aggressive and, without treatment, the tumors are often fatal within weeks. The majority of dog lymphomas are DLBCL and most of the others are T-cell lymphomas. Given the similarities of dog and human lymphomas, prior to initiating

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clinical trials of Selinexor in humans, we investigated a closely-related, orally available SINE, Verdinexor (KPT-335), in dogs with lymphomas. We have received a Minor Use / Minor Species, or MUMS, designation from the Center for Veterinary Medicine, or CVM, of the FDA for the treatment of newly-diagnosed or first relapse after chemotherapy lymphomas in dogs with Verdinexor.

Several different dog tumor cell lines including those derived from lymphomas exhibited growth inhibition and apoptosis *in vitro* upon exposure to nanomolar concentrations of Verdinexor. A Phase 1 clinical trial of Verdinexor was performed in dogs with cancer, primarily with lymphoma. The maximum tolerated dose was 35 mg/m² twice per week although biological activity was observed at 20 mg/m². PR or SD, in each case for at least 4 weeks, was observed in nine out of 14 dogs (64%) with lymphoma with a median time to disease progression of 66 days (range of 35 to 256 days). We performed a dose expansion study in six dogs with lymphoma who were given 30 mg/m² of Verdinexor three times per week; PR or SD was observed in four of the six dogs (67%) with a median time to disease progression of 83 days (range of 35 to 250 days). Side effects included anorexia, weight loss, vomiting and diarrhea and were manageable with dose modulation and supportive care. We conducted an owner observation-based survey and the data indicated that the overall quality of life did not change significantly in dogs treated with Verdinexor. Based on these findings, a Phase 2b clinical trial, intended to support regulatory approval under the MUMS designation in the United States, was performed in 58 pet dogs with either newly-diagnosed or first relapse after chemotherapy lymphomas. Verdinexor was administered initially at doses ranging from 25 mg/m² to 30 mg/m² two or three days per week. Minimal or no supportive care was given. The total CRs and PRs of the 58 dogs was 34%, with one CR and 19 PRs. An additional 33 of 58 dogs (57%) experienced SD for at least four weeks. The median time to disease progression was approximately five weeks, with 20 dogs (34%) remaining on study for longer than eight weeks. A few dogs who have received Verdinexor in the Phase 1 or 2b studies remained on therapy for longer than eight months.

We submitted the safety and effectiveness sections of a NADA for Verdinexor to the FDA in December 2013. We expect to seek to enter into a collaboration with a third party for the commercialization of Verdinexor for dog lymphoma, if we obtain regulatory approval. We believe that Verdinexor, if approved, would represent the first oral, targeted therapy for the treatment of dog lymphoma.

The evidence of anti-cancer activity and adverse effect profile of our drug candidate Verdinexor in dogs with certain NHL, primarily B and T-cell lymphomas, provided support for our decision to move our closely-related drug candidate Selinexor into Phase 1 clinical trials in humans.

Our Drug Discovery and Optimization Platform

The development of Selinexor, and other drug candidates, including our other SINE compounds and PAK4 inhibitors, as well as Verdinexor, began with our proprietary drug discovery and optimization platform. We intend to continue using this platform, which includes expertise in computational chemistry, our proprietary virtual chemical library and *in silico* screening know-how, certain biochemical assays, and *in silico* complexes of the structures of the target proteins bound with our small molecules, and other trade secrets and know-how.

While our platform can be used to target many protein families, we are focused on the discovery and development of novel inhibitors of nuclear export, particularly those targeting XPO1 and XPO1 cargos. We identified our small molecule inhibitors by using structural insights from X-ray crystallography and molecular modeling approaches, coupled with virtual screening. Initially promising compounds were then evaluated with our proprietary platform to optimize them into drug candidates.

Our ideal drug candidates selectively bind to the target protein and do so in part by forming a covalent bond with a particular cysteine residue in the protein. Cysteine is one of the 20 amino acids that make up proteins and has been useful for forming covalent bonds with drug compounds. Like

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non-covalent drugs, our compounds selectively bind, or "fit" into a specific binding pocket in the target protein, and don't "fit" well into binding pockets of other proteins. Additionally, our drug candidates form a covalent bond, which introduces a second level of selectivity, meaning that our compounds are less likely to bind inappropriately compared with typical non-covalent drugs. In addition, because covalent drugs can be given infrequently (e.g., once a day or even less), there are potentially fewer off-target effects as there is less need to maintain high drug levels. For example, Selinexor is now administered twice weekly.

Intellectual Property

Our commercial success depends in part on our ability to obtain and maintain proprietary or intellectual property protection for our drug candidates, our core technologies, and other know-how, to operate without infringing on the proprietary rights of others and to prevent others from infringing our proprietary or intellectual property rights. Our policy is to seek to protect our proprietary and intellectual property position by, among other methods, filing patent applications in the United States and in foreign jurisdictions related to our proprietary technology and drug candidates. We also rely on trade secrets, know-how and continuing technological innovation to develop and maintain our proprietary and intellectual property position.

We file patent applications directed to the composition of matter and methods of use and manufacture for our drug candidates. As of March 19, 2014, we were the sole owner of one patent in the United States (issued August 20, 2013 as U.S. Patent No. 8,513,230 and having an expiration date of March 5, 2031) and we had 20 pending patent applications in the United States, four pending international applications filed under the Patent Cooperation Treaty (PCT), one of which is co-owned with a third party, and 59 pending patent applications in foreign jurisdictions. The PCT is an international patent law treaty that provides a unified procedure for filing a single initial patent application to seek patent protection for an invention simultaneously in each of the member states. Although a PCT application is not itself examined and cannot issue as a patent, it allows the applicant to seek protection in any of the member states through national-phase applications. The technology underlying such pending patent applications has been developed by us and was not acquired from any in-licensing agreement.

The intellectual property portfolios for our key drug candidates as of March 19, 2014 are summarized below.

Selinexor (KPT-330): Our Selinexor patent portfolio covers the composition of matter and methods of use of Selinexor, as well as methods of making Selinexor, and consists of 26 pending foreign patent applications and two pending non-provisional applications in the United States. Any patents that may issue in the United States as part of our Selinexor patent portfolio will expire in 2032, absent any terminal disclaimer, patent term adjustment due to administrative delays by the United States Patent and Trademark Office, or USPTO, or patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Act. Any patents that may issue in foreign jurisdictions will likewise expire in 2032.

Selinexor (Wound Healing): Our patent portfolio covering Selinexor for wound healing covers methods of using Selinexor or Verdinexor for wound healing, and consists of one pending PCT patent application that provides the opportunity for seeking protection in all PCT member states. Any patents that may issue in the United States based on this PCT application will expire in 2034, absent any terminal disclaimer, patent term adjustment due to administrative delay by the USPTO or patent term extension under the Hatch-Waxman Act. Any patents issued in foreign jurisdictions will likewise expire in 2034.

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KPT-350: Our KPT-350 patent portfolio covers both the composition of matter and methods of use of KPT-350, and consists of one pending non-provisional U.S. patent application and one PCT application that provides the opportunity for seeking protection in all PCT member states. Any patents that may issue in the United States as part of our KPT-350 patent portfolio will expire in 2033, absent any terminal disclaimer, patent term adjustment due to administrative delays by the USPTO or patent term extension under the Hatch-Waxman Act. Any patents issued in foreign jurisdictions will likewise expire in 2033.

PAK4 Inhibitors: Our PAK4 patent portfolio covers both the composition of matter and methods of use of the PAK4 inhibitors described therein and consists of three patent families with nine pending U.S. provisional patent applications and one PCT application in total. The PCT Application provides the opportunity for seeking protection in all PCT member states in one family. Any patents that may issue in the United States based on this PCT application will expire in 2033, absent any terminal disclaimer, patent term adjustment due to administrative delays by the USPTO or patent term extension under the Hatch-Waxman Act. Any patents issued in foreign jurisdictions will likewise expire in 2033. We expect to file non-provisional patent applications claiming the benefit of the provisional applications in the second and third families in the second half of 2014. Any patents that may issue from such applications will expire no earlier than 2034.

Verdinexor (KPT-335): Our Selinexor patent portfolio described above also covers both the composition of matter and methods of use of Verdinexor, as well as methods of making Verdinexor.

In addition to the patent portfolios covering our key drug candidates, as of March 19, 2014, our patent portfolio also includes one patent that was issued August 20, 2013 as U.S. Patent No. 8,513,230 and pending patent applications relating to other XPO1 inhibitors and their use in targeted therapeutics. We also filed three Intent to Use Trademark Applications on August 29, 2013 covering our name, our logo and the two used together.

The term of individual patents depends upon the legal term for patents in the countries in which they are obtained. In most countries, including the United States, the patent term is 20 years from the earliest filing date of a non-provisional patent application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the USPTO in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier filed patent. The term of a patent that covers a drug may also be eligible for patent term extension when FDA approval is granted, provided statutory and regulatory requirements are met. See " Government Regulation Patent Term Restoration and Extension" below for additional information on such extensions. In the future, if and when our drug candidates receive approval by the FDA or foreign regulatory authorities, we expect to apply for patent term extensions on issued patents covering those drugs, depending upon the length of the clinical trials for each drug candidate and other factors. There can be no assurance that any of our pending patent applications will issue or that we will benefit from any patent term extension or favorable adjustment to the term of any of our patents.

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As with other biotechnology and pharmaceutical companies, our ability to maintain and solidify our proprietary and intellectual property position for our drug candidates and technologies will depend on our success in obtaining effective patent claims and enforcing those claims if granted. However, patent applications that we may file or license from third parties may not result in the issuance of patents. We also cannot predict the breadth of claims that may be allowed or enforced in our patents. Our issued patent and any issued patents that we may receive in the future may be challenged, invalidated or circumvented. For example, we cannot be certain of the priority of inventions covered by pending third-party patent applications. If third parties prepare and file patent applications that also claim technology or therapeutics to which we have rights, we may have to participate in interference proceedings to determine priority of invention, which could result in substantial costs to us, even if the eventual outcome is favorable to us. In addition, because of the extensive time required for clinical development and regulatory review of a drug candidate we may develop, it is possible that, before any of our drug candidates can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby reducing any advantage of any such patent.

In addition to patents, we rely upon unpatented trade secrets and know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, using confidentiality agreements with our collaborators, scientific advisors, employees and consultants, and invention assignment agreements with our employees. We also have agreements with selected consultants, scientific advisors and collaborators requiring assignment of inventions. The confidentiality agreements are designed to protect our proprietary information and, in the case of agreements or clauses requiring invention assignment, to grant us ownership of technologies that are developed through our relationship with a third party.

With respect to our proprietary drug discovery and optimization platform, we consider trade secrets and know-how to be our primary intellectual property. Trade secrets and know-how can be difficult to protect. We anticipate that with respect to this technology platform, these trade secrets and know-how may over time be disseminated within the industry through independent development, the publication of journal articles describing the methodology, and the movement of personnel skilled in the art from academic to industry scientific positions.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technology, knowledge, experience and scientific resources provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Any drug candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

There are a large number of companies developing or marketing treatments for cancer and the other indications on which we currently plan to initially focus, including many major pharmaceutical and biotechnology companies. However, to our knowledge, no other company has an XPO1 inhibitor in clinical development at the present time.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant

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competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or that may be necessary for, our programs.

The key competitive factors affecting the success of all of our drug candidates, if approved, are likely to be their efficacy, safety, convenience, price, the level of generic competition and the availability of reimbursement from government and other third-party payors.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize drugs that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any drugs that we may develop. Our competitors also may obtain FDA or other regulatory approval for their drugs more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic drugs. Generic drugs for the treatment of cancer and the other indications on which we currently plan to initially focus are currently on the market, and additional drugs are expected to become available on a generic basis over the coming years. If we obtain marketing approval for our drug candidates, we expect that they will be priced at a significant premium over competitive generic drugs.

The most common methods of treating patients with cancer are surgery, radiation and drug therapy. There are a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. While our drug candidates may compete with many existing drugs and other therapies, to the extent they are ultimately used in combination with or as an adjunct to these therapies, our drug candidates will not be competitive with them. Some of the currently-approved drug therapies are branded and subject to patent protection, and others are available on a generic basis. Many of these approved drugs are well-established therapies and are widely-accepted by physicians, patients and third-party payors.

In addition to currently-marketed therapies, there are also a number of drugs in late stage clinical development to treat cancer and the other indications on which we plan to initially focus. These drugs in development may provide efficacy, safety, convenience and other benefits that are not provided by currently-marketed therapies. As a result, they may provide significant competition for any of our drug candidates for which we obtain marketing approval.

If our lead drug candidates are approved for the indications for which we currently plan to initially focus, they will compete with the therapies and currently-marketed drugs discussed below.

XPO1 Inhibitors

We have observed preliminary evidence of anti-cancer activity of our XPO1 inhibitor and lead drug candidate, Selinexor, across a spectrum of patients with advanced cancers who had received multiple previous treatments and, despite these treatments, had disease that was progressing at the time of enrollment in our clinical trials. Assuming continued positive results from our ongoing Phase 1 and Phase 2 clinical trials of Selinexor and pending regulatory feedback, we plan to initiate registration-directed clinical trials of Selinexor in three hematological malignancy indications during 2014. We expect to initiate these clinical trials for Selinexor in AML, DLBCL and Richter's Syndrome. We plan to seek regulatory approvals of Selinexor in North America and Europe in each such indication with respect to which we receive positive clinical trial results and positive regulatory feedback. We may seek such approvals in other geographies as well. In solid tumor malignancies, we have initiated Phase 2 clinical trials of Selinexor in relapsed glioblastoma multiforme and in ovarian, cervical and uterine carcinomas and expect to initiate Phase 2 clinical trials in squamous head, neck or lung cancers and hormone and chemotherapy refractory metastatic prostate cancer during 2014.

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Patients with AML typically are treated with intensive multi-agent chemotherapy and high risk patients who enter remission and have a matched donor often receive an allogeneic stem cell transplant. Elderly patients with AML are often treated with less intensive chemotherapy regimens or drugs called hypomethylating agents because usual chemotherapy has marked toxicities. Once elderly patients with AML experience disease progression while on their initial chemotherapy and/or hypomethylating agent, their expected survival is very poor. Because of their advanced age, multiple other medical conditions, and requirements for multiple other drugs, the treatment of relapsed and/or refractory AML in elderly persons is difficult. An IL3-toxin conjugate (Stemline Inc.) is being evaluated in elderly persons with relapsed and/or refractory AML. A number of other trials with existing anti-cancer drugs (often in combinations) are ongoing in this population.

The initial therapy for DLBCL typically consists of multi-agent cytotoxic drugs in combination with the monoclonal antibody rituximab (Rituxan®). In patients with DLBCL who are not elderly and who have good organ function, high dose chemotherapy with stem cell transplantation is often used. Newer targeted agents such as the BTK inhibitor ibrutinib and the immunomodulatory drug lenalidomide (Revlimid®) have shown activity in immunoblastic (activated B cell) DLBCL. There are also a number of other widely-used anti-cancer agents that have broad labels which include NHL, and some of these are being evaluated alone or in combination for the treatment of patients with DLBCL that have relapsed after several different types of chemotherapy. Certain monoclonal antibodies similar to rituximab are also being evaluated in relapsed DLBCL.

Although there are no specific therapies approved to treat Richter's Syndrome, multi-agent chemoimmunotherapy is typically used as a first line treatment.

Currently, there are three commonly-used targeted or novel agents approved in the U.S. for the treatment of patients with MM: Velcade®, Revlimid® and Thalomid®. Other approved agents include Kyprolis®, approved by the FDA on July 20, 2012, and Pomalyst®, approved by the FDA on February 8, 2013, each for the relapsed and/or refractory patient population. Other potentially competitive therapies are in clinical development for MM. Vorinostat, being developed by Merck & Co., and panobinostat, being developed by Novartis AG, are being studied in combination with bortezomib for relapsed myeloma, and elotuzumab is being developed by Abbott Laboratories.

Drug compounds currently in preclinical studies, if developed and approved, could also be competitive with our drug candidates, if approved. Kosan Biosciences Inc. (acquired by Bristol-Myers Squibb Company) has evaluated compounds derived from leptomyacin B in preclinical studies. CanBas Co., Ltd. has been developing a product referred to as CBS9106, a preclinical XPO1 inhibitor.

With respect to indications other than cancer, there are many currently- marketed therapies and drugs in late-stage clinical development to treat non-oncology indications on which we plan to initially focus development of our XPO1 inhibitors. However, to our knowledge, as in cancer, there are no other XPO1 inhibitors in clinical development for the treatment of any other diseases, including indications like autoimmune and inflammatory diseases or wound healing. There is no published information on the use of the preclinical compounds that have been developed by Kosan Biosciences or CanBas Co. in models other than cancer.

PAK4 Inhibitors

Our PAK4 inhibitors, if developed and approved, would compete with currently- marketed therapies and drugs in clinical development to treat cancer. However, there are currently no marketed therapies that selectively target PAK4. Pfizer Inc. developed PF-03758309, a non-selective PAK inhibitor, meaning that this compound inhibited several of the PAK family members, and not solely PAK4, through Phase 1 clinical development, but that compound had poor oral bioavailability and, to our knowledge, its development has been discontinued. We are aware that PAK4 biology is being

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evaluated preclinically by AstraZeneca plc and Genentech, Inc. (acquired by Roche Holding AG). We are not aware of any PAK4 inhibitors that are in clinical development at the present time.

Manufacturing

We do not have any manufacturing facilities or personnel. We currently rely, and expect to continue to rely, on third parties for the manufacture of our drug candidates for preclinical and clinical testing, as well as for commercial manufacture if our drug candidates receive marketing approval. We have engaged one third party manufacturer to obtain the active pharmaceutical ingredient for Selinexor for preclinical and clinical testing. We have engaged a separate third-party manufacturer for fill-and-finish services. We obtain our supplies from these manufacturers on a purchase order basis and do not have a long-term supply arrangement in place. We do not currently have arrangements in place for redundant supply. For all of our drug candidates, we intend to identify and qualify additional manufacturers to provide the active pharmaceutical ingredient and fill-and-finish services prior to seeking regulatory approval.

All of our drug candidates are small molecules and are manufactured in reliable and reproducible synthetic processes from readily available starting materials. The chemistry is amenable to scale up and does not require unusual equipment in the manufacturing process. We expect to continue to develop drug candidates that can be produced cost-effectively at contract manufacturing facilities.

Government Regulation

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, and import and export of pharmaceutical products. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

Review and Approval of Drugs in the United States

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval may subject an applicant and/or sponsor to a variety of administrative or judicial sanctions, including refusal by FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by FDA and the Department of Justice, or DOJ, or other governmental entities.

An applicant seeking approval to market and distribute a new drug product in the United States must typically undertake the following:

completion of preclinical laboratory tests, animal studies and formulation studies in compliance with FDA's good laboratory practice, or GLP, regulations;

submission to FDA of an investigational new drug application, or IND, which must take effect before human clinical trials may begin;

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approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;

performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug product for each indication;

preparation and submission to FDA of a new drug application, or NDA;

review of the product by an FDA advisory committee, where appropriate or if applicable;

satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with current Good Manufacturing Practices, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;

payment of user fees and securing FDA approval of the NDA; and

compliance with any post-approval requirements, including Risk Evaluation and Mitigation Strategies, or REMS, and post-approval studies required by FDA.

Preclinical Studies

Preclinical studies include laboratory evaluation of the purity and stability of the manufactured drug substance or active pharmaceutical ingredient and the formulated drug or drug product, as well as *in vitro* and animal studies to assess the safety of the drug for initial testing in humans and to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. The results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical studies, among other things, are submitted to FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted.

Human Clinical Studies in Support of an NDA

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. An IND automatically becomes effective 30 days after receipt by FDA, unless before that time the FDA raises concerns or questions related to a proposed clinical trial and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin.

In addition, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health for public dissemination on their ClinicalTrials.gov website.

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Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined:

- Phase 1: The drug is initially introduced into healthy human subjects or patients with the target disease (e.g. cancer) or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.
- Phase 2: The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- Phase 3: The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

Section 505(b)(2) NDAs

NDAs for most new drug products are based on two full clinical studies which must contain substantial evidence of the safety and efficacy of the proposed new product. These applications are submitted under Section 505(b)(1) of the FDCA. The FDA is, however, authorized to approve an alternative type of NDA under Section 505(b)(2) of the FDCA. This type of application allows the applicant to rely, in part, on the FDA's previous findings of safety and efficacy for a similar product, or published literature. Specifically, Section 505(b)(2) applies to NDAs for a drug for which the investigations made to show whether or not the drug is safe for use and effective in use and relied upon by the applicant for approval of the application "were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted."

Thus, Section 505(b)(2) authorizes the FDA to approve an NDA based on safety and effectiveness data that were not developed by the applicant. NDAs filed under Section 505(b)(2) may provide an alternate and potentially more expeditious pathway to FDA approval for new or improved formulations or new uses of previously approved products. If the 505(b)(2) applicant can establish that reliance on the FDA's previous approval is scientifically appropriate, the applicant may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new drug candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

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Submission of an NDA to FDA

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to FDA as part of an NDA requesting approval to market the drug product for one or more indications. Under federal law, the submission of most NDAs is additionally subject to an application user fee, currently exceeding \$2.1 million, and the sponsor of an approved NDA is also subject to annual product and establishment user fees, currently exceeding \$104,000 per product and \$554,600 per establishment. These fees are typically increased annually.

The FDA conducts a preliminary review of an NDA within 60 days of its receipt and informs the sponsor by the 74th day after FDA's receipt of the submission to determine whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before FDA accepts it for filing. Once the submission is accepted for filing, FDA begins an in-depth substantive review. The FDA has agreed to specified performance goals in the review process of NDAs. Most such applications are meant to be reviewed within ten months from the date of filing, and most applications for "priority review" products are meant to be reviewed within six months of filing. The review process may be extended by FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by FDA following the original submission.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP.

The FDA also may require submission of a REMS plan to mitigate any identified or suspected serious risks. The REMS plan could include medication guides, physician communication plans, assessment plans, and elements to assure safe use, such as restricted distribution methods, patient registries, or other risk minimization tools.

The FDA is required to refer an application for a novel drug to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Fast Track Designation

The FDA is authorized to expedite the review of applications for new drug products that are intended, either alone or in combination with other products, for the treatment of a serious or life-threatening disease or condition for which there is no effective treatment and which demonstrate the potential to address unmet medical needs for the disease or condition. Under the fast track program, the sponsor of a drug candidate may request FDA to designate the product for a specific indication as a fast track product concurrent with or after the filing of the IND for the drug candidate. The FDA must determine if the drug candidate qualifies for fast track designation within 60 days after receipt of the sponsor's request.

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In addition to other benefits, such as the ability to use surrogate endpoints and have greater interactions with FDA, FDA may initiate review of sections of a fast track product's NDA before the application is complete. This rolling review is available if the applicant provides, and FDA approves, a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, FDA's time period goal for reviewing a fast track application does not begin until the last section of the NDA is submitted. In addition, the fast track designation may be withdrawn by FDA if FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Breakthrough Therapies

In 2012, Congress enacted the Food and Drug Administration Safety and Improvement Act or FDASIA. This law established a new regulatory scheme allowing for expedited review of products designated as "breakthrough therapies." Breakthrough therapies are defined as those intended, either alone or in combination with other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development.

Under FDASIA, FDA may take certain actions with respect to products designated as breakthrough therapies, including holding meetings with the sponsor and the review team throughout the development process; providing timely advice to and communication with the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking certain steps to design the clinical trials in an efficient manner.

Accelerated Approval

FDASIA also codified and expanded on FDA's accelerated approval regulations, under which FDA may approve a drug for a serious or life-threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit. Under FDASIA, FDA may also grant accelerated approval using a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments.

A surrogate endpoint is a measurement of laboratory or clinical signs of a disease or condition that substitutes for a direct measurement of how a patient feels, functions or survives. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. FDASIA lists the types of evidence that may be used to support a finding that an endpoint is reasonably likely to predict clinical benefit. A drug candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

FDA's Decision on an NDA

On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order

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for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess the drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;

fines, warning letters or holds on post-approval clinical trials;

refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;

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product seizure or detention, or refusal to permit the import or export of products; or

injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Act, Congress authorized the FDA to approve generic drugs that are the same as drugs previously approved by the FDA under the NDA provisions of the statute. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application or ANDA to the agency. In support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference listed drug, or RLD.

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, and the strength of the drug. At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if "the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug. . . ."

Upon approval of an ANDA, the FDA indicates that the generic product is "therapeutically equivalent" to the RLD and it assigns a therapeutic equivalence rating to the approved generic drug in its publication "Approved Drug Products with Therapeutic Equivalence Evaluations," also referred to as the "Orange Book." Physicians and pharmacists consider an "AB" therapeutic equivalence rating to mean that a generic drug is fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, FDA's designation of an "AB" rating often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity. In cases where such exclusivity has been granted, an ANDA may not be filed with FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval. The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication.

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Hatch-Waxman Patent Certification and the 30-Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or an approved method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an ANDA applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval. To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would.

Specifically, the applicant must certify with respect to each patent that:

the required patent information has not been filed;

the listed patent has expired;

the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or

the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicate that it is not seeking approval of a patented method of use, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired.

If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months after the receipt of the Paragraph IV notice, expiration of the patent, or a decision in the infringement case that is favorable to the ANDA applicant.

Pediatric Studies and Exclusivity

Under the Pediatric Research Equity Act of 2003, a NDA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the drug product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. With enactment of the Food and Drug Administration Safety and Innovation Act, or FDASIA, in 2012, sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The applicant, FDA, and FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in FDASIA. Unless otherwise

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required by regulation, the pediatric data requirements do not apply to products with orphan designation.

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot accept or approve another application.

Orphan Designation and Exclusivity

Under the Orphan Drug Act, FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition (generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for treatment of the disease or condition will be recovered from sales of the product). A company must request orphan product designation before submitting a NDA. If the request is granted, FDA will disclose the identity of the therapeutic agent and its potential use. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product with orphan status receives the first FDA approval for the disease or condition for which it has such designation, the product will be entitled to orphan product exclusivity. Orphan product exclusivity means that FDA may not approve any other applications for the same product for the same indication for seven years, except in certain limited circumstances. Competitors may receive approval of different products for the indication for which the orphan product has exclusivity and may obtain approval for the same product but for a different indication. If a drug or drug product designated as an orphan product ultimately receives marketing approval for an indication broader than what was designated in its orphan product application, it may not be entitled to exclusivity.

Patent Term Restoration and Extension

A patent claiming a new drug product may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted is typically one-half the time between the effective date of an IND and the submission date of a NDA, plus the time between the submission date of a NDA and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved drug product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple drugs for which approval is sought can only be extended in connection with one of the approvals. The USPTO reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Review and Approval of Drug Products in the European Union

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality,

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safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of drug products. Whether or not it obtains FDA approval for a product, the company would need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. The approval process ultimately varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Pursuant to the European Clinical Trials Directive, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the member states. Under this system, an applicant must obtain approval from the competent national authority of a European Union member state in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial after a competent ethics committee has issued a favourable opinion. Clinical trial application must be accompanied by an investigational medicinal product dossier with supporting information prescribed by the European Clinical Trials Directive and corresponding national laws of the member states and further detailed in applicable guidance documents.

To obtain marketing approval of a drug under European Union regulatory systems, an applicant must submit a marketing authorization application, or MAA, either under a centralized or decentralized procedure.

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all European Union member states. The centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional.

Under the centralized procedure, the Committee for Medicinal Products for Human Use, or the CHMP, established at the European Medicines Agency, or EMA, is responsible for conducting the initial assessment of a drug. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. In this circumstance, the EMA ensures that the opinion of the CHMP is given within 150 days.

The decentralized procedure is available to applicants who wish to market a product in various European Union member states where such product has not received marketing approval in any European Union member states before. The decentralized procedure provides for approval by one or more other, or concerned, member states of an assessment of an application performed by one member state designated by the applicant, known as the reference member state. Under this procedure, an applicant submits an application based on identical dossiers and related materials, including a draft summary of product characteristics, and draft labeling and package leaflet, to the reference member state and concerned member states. The reference member state prepares a draft assessment report and drafts of the related materials within 210 days after receipt of a valid application. Within 90 days of

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receiving the reference member state's assessment report and related materials, each concerned member state must decide whether to approve the assessment report and related materials.

If a member state cannot approve the assessment report and related materials on the grounds of potential serious risk to public health, the disputed points are subject to a dispute resolution mechanism and may eventually be referred to the European Commission, whose decision is binding on all member states.

Data and Market Exclusivity in the European Union

In the European Union, new chemical entities qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. This data exclusivity, if granted, prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic (abbreviated) application for eight years, after which generic marketing authorization can be submitted, and the innovator's data may be referenced, but not approved for two years. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity and the sponsor is able to gain the prescribed period of data exclusivity, another company nevertheless could also market another version of the drug if such company can complete a full MAA with a complete database of pharmaceutical test, pre-clinical tests and clinical trials and obtain marketing approval of its product.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of products approved by FDA and other government authorities. Sales of products will depend, in part, on the extent to which the costs of the products will be covered by third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. A payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Third-party reimbursement may not be sufficient to maintain price levels high enough to realize an appropriate return on investment in product development.

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of drugs have been a focus in this effort. Third-party payors are increasingly challenging the prices charged for medical products and services and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. If these third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover the product after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid health care costs,

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including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. Adoption of such controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals.

As a result, the marketability of any product which receives regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, an increasing emphasis on managed care in the United States has increased and will continue to increase the pressure on drug pricing. Coverage policies, third-party reimbursement rates and drug pricing regulation may change at any time. In particular, the Patient Protection and Affordable Care Act contains provisions that may reduce the profitability of drug products, including, for example, increased rebates for drugs sold to Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal health care programs. Even if favorable coverage and reimbursement status is attained for one or more products that receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that drug products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular drug candidate to currently available therapies. For example, the European Union provides options for its member states to restrict the range of drug products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a drug product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the drug product on the market. Other member states allow companies to fix their own prices for drug products, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert competitive pressure that may reduce pricing within a country. Any country that has price controls or reimbursement limitations for drug products may not allow favorable reimbursement and pricing arrangements.

Healthcare Law and Regulation

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with third-party payors and customers are subject to broadly applicable fraud and abuse and other healthcare laws and regulations. Such restrictions under applicable federal and state healthcare laws and regulations, include the following:

the federal healthcare Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;

the federal False Claims Act imposes civil penalties, and provides for civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or

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making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;

the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

the federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;

the federal transparency requirements under the Health Care Reform Law will require manufacturers of drugs, devices and medical supplies to report to the Department of Health and Human Services information related to payments and other transfers of value to physicians and teaching hospitals and physician ownership and investment interests; and

analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Review and Approval of Animal Drugs in the United States

In addition to pursuing approval of our drug candidates for use in human beings, we may also seek approval of certain drug candidates for veterinary applications. As with new drug products for human beings, new animal drugs may not be marketed in the United States until they have been approved by the FDA as safe and effective. The requirements and phases governing approval of a new animal drug are analogous to those for new human drugs. Specifically, the Center for Veterinary Medicine or CVM at FDA is responsible for determining whether a new veterinary product should be approved on the basis of a NADA filed by the applicant. A NADA must contain substantial evidence of the safety and effectiveness of the animal drug, as well as data and controls demonstrating that the product will be manufactured and studied in compliance with, among other things, applicable cGMP and GLP practices.

To begin this process, an applicant must file an Investigational New Animal Drug application, or INAD, with the CVM. The applicant will hold a pre- development meeting with the CVM to reach general agreement on the plans for providing the data necessary to fulfill requirements for a NADA. In this context, an applicant must submit pivotal protocols to the CVM for review and concurrence prior

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to conducting the required studies. The applicant will gather and submit data on safety, efficacy and chemistry, manufacturing and controls or CMC to the CVM for review, as below:

Safety:	The design and review of the safety study and the study protocol are completed prior to initiation of the study to help assure that the data generated will meet FDA requirements. These studies are conducted under rigorous quality control, including GLP, to assure integrity of the data. They are designed to clearly define a safety margin, identify any potential safety concerns, and establish a safe dose for the product. This dose and effectiveness is then evaluated in the pivotal field efficacy study where the product is studied in the animal patient population in which the product is intended to be used.
Efficacy:	Early pilot studies may be done in laboratory cats or dogs to establish effectiveness and the dose range for each product. When an effective dose is established, a study protocol to test the product in real world conditions is developed prior to beginning the study. The pivotal field efficacy study protocol is submitted for review and concurrence prior to study initiation, to help assure that the data generated will meet requirements. This study must be conducted with the formulation of the product that is intended to be commercialized, and is a multi-site, randomized, controlled study, generally with a placebo control.
CMC:	To assure that the new animal drug product can be manufactured consistently, FDA will require applicants to provide documentation of the process by which the active ingredient is made and the controls applicable to that process that assure the active ingredient and the formulation of the final commercial product meet certain criteria, including purity and stability. After a product is approved, applicants will be required to communicate with FDA before any changes are made to these procedures or at the manufacturing site. Both the active ingredient and commercial formulations are required to be manufactured at facilities that practice cGMP.

Once all data have been submitted and reviewed for each technical section - safety, efficacy and CMC the CVM will issue a technical section complete letter as each section review is completed. When the three letters have been issued, the applicant will compile a draft of the Freedom of Information Summary, the proposed labeling, and all other relevant information, and submit these as an administrative NADA for CVM review. Generally, if there are no deficiencies in the submission, the NADA will be issued within four to six months after submission of the administrative NADA. This review will be conducted according to timelines specified in the Animal Drug User Fee Act. The FDA's basis for approving a NADA is documented in a Freedom of Information Summary. Post-approval monitoring of products is required by law, with reports being provided to the CVM's Surveillance and Compliance group. Reports of product quality defects, adverse events or unexpected results must also be produced in accordance with the relevant regulatory requirements.

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Employees

As of February 28, 2014, we had 31 full-time employees, including a total of 13 employees with M.D. or Ph.D. degrees. Of these full-time employees, 25 employees are engaged in research and development activities. None of our employees is represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

Facilities

We occupy approximately 7,743 square feet of office and laboratory space in Natick, Massachusetts under a lease that expires in January 31, 2015. In order to accommodate our anticipated need for additional office and laboratory space, we intend to enter into an agreement to lease approximately 30,000 square feet of office and laboratory space in Newton, Massachusetts.

Legal Proceedings

We are not currently a party to any material legal proceedings.

Table of Contents**MANAGEMENT****Executive Officers and Directors**

The following table sets forth the name, age and position of each of our executive officers and directors as of March 1, 2014.

Name	Age	Position
Executive Officers		
Michael G. Kauffman, M.D., Ph.D.(3)	50	Chief Executive Officer and Director
Sharon Shacham, Ph.D., M.B.A.	43	President and Chief Scientific Officer
Paul Brannelly	41	Senior Vice President, Finance and Administration, Secretary and Treasurer
Directors		
Garen G. Bohlin(1)(3)	66	Director
Barry E. Greene(1)(2)	50	Director
Deepa R. Pakianathan, Ph.D.(1)(2)	49	Director
Mansoor Raza Mirza, M.D.	52	Director
Kenneth E. Weg(2)(3)	75	Director

- (1) Member of the audit committee.
- (2) Member of the compensation committee.
- (3) Member of the nominating and corporate governance committee.

Michael G. Kauffman, M.D., Ph.D. Dr. Kauffman has served as Karyopharm's Chief Executive Officer since January 2011 and has been one of our directors since 2008. Dr. Kauffman co-founded Karyopharm with Dr. Sharon Shacham in 2008 and served as President from January 2011 to December 2013 and as Chief Medical Officer from December 2012 to December 2013. Prior to joining Karyopharm, he was Chief Medical Officer of Onyx Pharmaceuticals Inc., a biopharmaceutical company, from November 2009 to December 2010, which acquired Proteolix Inc. in November 2009 where he was Chief Medical Officer since November 2008, where he led the development of Kyprolis® (carfilzomib), a novel proteasome inhibitor approved in refractory myeloma by the FDA in July 2012. Prior to joining Onyx Pharmaceuticals, Dr. Kauffman was an operating partner at Bessemer Venture Partners from 2006 to 2008 where he led investments in biotechnology companies. Prior to that, he was President and Chief Executive Officer of Epix Pharmaceuticals, Inc., a biopharmaceutical company that underwent liquidation proceedings through an assignment for the benefit of creditors under Massachusetts law in 2009, from 2006 to 2008, and President and Chief Executive Officer of Predix Pharmaceuticals, Inc., a private biopharmaceutical company focused on G protein-coupled receptors (GPCR), from 2002 until its merger into Epix Pharmaceuticals in 2006, where he led the merger of Predix Pharmaceuticals and Epix Pharmaceuticals, oversaw the discovery and development of four new clinical candidates and led collaboration transactions with Amgen and GlaxoSmithKline. From March 2000 to September 2002, Dr. Kauffman was Vice President, Clinical at Millennium Pharmaceuticals, Inc., a biopharmaceutical company, where he led the Velcade® development program. From September 1997 to March 2000, Dr. Kauffman held a number of senior positions at Millennium Predictive Medicine, Inc., a biopharmaceutical company and a subsidiary of Millennium Pharmaceuticals, where he led the discovery and development of novel molecular diagnostics for major cancers including melanoma, and led transactions with Becton-Dickenson and Bristol Myers Squibb. From August 1995 to September 1997, Dr. Kauffman held a number of senior positions at Biogen Idec, Inc., a biopharmaceutical company, where he led the clinical development of anti-CD40L antibodies in autoimmune and inflammatory diseases, and acted as the main medical advisor to the Biogen business development group. Dr. Kauffman currently serves on the board of directors and

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compensation committee of Verastem Inc., a public biopharmaceutical company, on the board of directors and the audit committee and compensation committee of Zalicus Inc. (formerly CombinatoRx Inc.), a public biopharmaceutical company, and on the board of directors and the compensation committee of Metamark Genetics Inc., a private molecular diagnostics company. Dr. Kauffman received his B.A. in Biochemistry from Amherst College, his M.D. and Ph.D. from Johns Hopkins Medical School, and trained in internal medicine and rheumatology at Beth Israel (now Beth Israel Deaconness Medical Center) and Massachusetts General Hospitals. He is board certified in internal medicine. We believe Dr. Kauffman's qualifications to serve on our board of directors include his extensive experience in the healthcare industry as well his extensive knowledge of our company and its business since inception through service in multiple executive leadership positions and as a member of our board.

Sharon Shacham, Ph.D., M.B.A. Dr. Shacham founded Karyopharm in 2008 and has served as our President since December 2013 and as our Chief Scientific Officer since October 2010. Dr. Shacham served as our President of Research and Development from December 2012 to December 2013, as our Head of Research and Development from October 2010 to December 2012 and as our President and Chief Executive Officer from October 2010 to January 2011. Dr. Shacham established the company to focus on the discovery and development of small molecule inhibitors of nuclear export and has led our scientific progress since inception. Her computational drug discovery algorithms formed a critical part of the technological basis for our drug discovery and optimization platform, which was used for the discovery of Selinexor, our lead drug candidate. Dr. Shacham co-chairs our Scientific Advisory Board. Prior to founding Karyopharm, from July 2000 to April 2009, she was Senior Vice President of Drug Development at Epix Pharmaceuticals, Inc., which underwent liquidation proceedings through an assignment for the benefit of creditors under Massachusetts law in 2009, and Director, Algorithm and Software Development at Predix Pharmaceuticals Inc. which merged into Epix Pharmaceuticals in 2006, where she led the company's efforts in GPCR modeling, computational chemistry, lead optimization and development of clinical trials. Dr. Shacham received her B.Sc. in Chemistry, Ph.D. and M.B.A. from Tel Aviv University.

Paul Brannelly. Mr. Brannelly joined Karyopharm in June 2013 as Senior Vice President, Finance and Administration and has served as our Treasurer since July 2013 and our Secretary from July 2013 until March 2014. Prior to joining Karyopharm, Mr. Brannelly served most recently as Vice President of Finance at Verastem, Inc., a biopharmaceutical company, from September 2011 to June 2013, Chief Financial Officer from November 2010 to September 2011, and as Treasurer and Secretary from November 2010 to June 2013, where he led the company through the initial public offering process and managed several successful financings. From January 2010 to September 2011, Mr. Brannelly held the position of Chief Financial Officer at the Longwood Fund, a venture capital firm aimed at investing in, managing and building healthcare companies, where he set up the financial and operational infrastructure following the closing of its first fund. From November 2005 to September 2009, he served as Vice President, Finance at Sirtris Pharmaceuticals, Inc., a biopharmaceutical company which GlaxoSmithKline plc purchased for \$720 million in 2008, where he managed the S-1 preparation and due diligence process for Sirtris' initial public offering and managed the company's transition to being a public company. Mr. Brannelly started his biopharmaceutical career at Dyax Corporation from September 1999 to May 2002, and subsequently moved on to positions of increasing responsibility at Zalicus Inc. (formerly CombinatoRx Inc.) from May 2002 to November 2005, most recently as VP Finance and Treasurer, where he led Zalicus through the initial public offering process. Mr. Brannelly holds a Bachelors of Business Administration in Accounting from the University of Massachusetts at Amherst.

Garen G. Bohlin. Garen G. Bohlin has served as a member of our board of directors since October 2013. Since April 2012, Mr. Bohlin has focused exclusively on service on boards of directors and consulting. From January 2010 until his retirement in April 2012, he served as Executive Vice

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President of Constellation Pharmaceuticals, Inc., a biopharmaceutical company, where his responsibilities included consummating option-to-acquire and pre-negotiated merger agreements with Genentech. Prior to Constellation Pharmaceuticals, Mr. Bohlin served as Chief Operating Officer of Sirtris Pharmaceuticals, a biotechnology company, from January 2006 to December 2009, where he played key roles in the overall management of Sirtris, its initial public offering and the sale of the company to GlaxoSmithKline. Mr. Bohlin was the founding Chief Executive Officer of Syntonix Pharmaceuticals, Inc., a biopharmaceutical company, from 1999 through December 2008, where he played a key role in the overall management of Syntonix, positioning it for an eventual sale to Biogen Idec. Prior to Syntonix, Mr. Bohlin was Executive Vice President of Genetics Institute Inc., a biotechnology company, where he played a key role in overall management, its initial public offering and its sale to American Home Products/Wyeth, and a partner at Arthur Andersen & Co., a public accounting and consulting organization. Mr. Bohlin serves on the board of directors and audit committees of Tetrphase Pharmaceuticals, Inc., a public biopharmaceutical company, and Acusphere, Inc., a public biotechnology company, and serves on the board of directors and audit committee of Precision Dermatology, Inc., a private biotechnology company. He holds a B.S. in Accounting from the University of Illinois. We believe Mr. Bohlin's qualifications to serve on our board of directors include his extensive industry and board experience, including his audit committee experience, with publicly traded and privately held biotechnology companies.

Barry E. Greene. Mr. Greene has served as a member of our board of directors since January 2013. Mr. Greene has served as President and Chief Operating Officer of Alnylam Pharmaceuticals, Inc., a biopharmaceutical company, since 2007, as its Chief Operating Officer since 2003, and from 2004 through 2005, as its Treasurer. Mr. Greene joined Alnylam in 2003, bringing over 15 years of experience in the healthcare industry and in consulting. Prior to Alnylam, he was General Manager of Oncology at Millennium Pharmaceuticals, Inc., a biopharmaceutical company, where he led the company's global strategy and execution for its oncology business, including strategic business direction and execution, culminating in the successful FDA approval and launch of VELCADE (bortezomib) in mid-2003. Prior to joining Millennium in 2001, Mr. Greene served as Executive Vice President and Chief Business Officer for Mediconsult.com, a healthcare consulting company. Prior to Mediconsult.com, Mr. Greene's experience included serving as Vice President of Marketing and Customer Services for AstraZeneca (formerly AstraMerck), a biopharmaceutical company; Vice President, Strategic Integration with responsibility for the AstraZeneca North American post-merger integration; and a partner of Andersen Consulting, a consulting company, where he was responsible for the pharmaceutical/biotechnology marketing and sales practice. Mr. Greene currently is a member of the board of directors of Acorda Therapeutics, Inc., a public biopharmaceutical company. Mr. Greene received his B.S. in Industrial Engineering from the University of Pittsburgh and serves as a Senior Scholar at Duke University, Fuqua School of Business. We believe Mr. Greene's qualifications to serve on our board of directors include his extensive experience in the healthcare and consulting industries as well his practical experience guiding new drugs through the commercialization process.

Deepa R. Pakianathan, Ph.D. Dr. Pakianathan has served as a member of our board of directors since April 2013. Since 2001, Dr. Pakianathan has been a Managing Member at Delphi Ventures, a venture capital firm focused on medical device and biotechnology investments, and leads the firm's biotechnology investment activities. From 1998 to 2001, Dr. Pakianathan was a senior biotechnology banker at JPMorgan, a global investment bank. Since 2004, Dr. Pakianathan has served on the board of directors of Alexza Pharmaceuticals, Inc., a public biopharmaceutical company, where she serves as a member of its compensation and nominating and governance committees. Since 2007, Dr. Pakianathan has served on the board of directors of Alder Biopharmaceuticals, Inc., a private biopharmaceutical company, where she serves as a member of its nominating and governance committee, and has served on the board of directors of NeurAxon, Inc., a private biopharmaceutical company, where she serves as a member of its compensation committee. Since 2008, Dr. Pakianathan has served on the board of directors of OncoMed Pharmaceuticals, Inc., a public biopharmaceutical

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company, where she serves as chair of its audit committee. From 2009 to February 2013, Dr. Pakianathan served on the board of directors of PTC Therapeutics, Inc., a public biopharmaceutical company. Dr. Pakianathan received a B.Sc. from the University of Bombay, India, a M.Sc. from The Cancer Research Institute at the University of Bombay, India, and an M.S. and Ph.D. from Wake Forest University. We believe Dr. Pakianathan's qualifications to serve on our board of directors include her experience as a venture capital investor in, and director of, multiple biotechnology companies, as well as her experience as a biotechnology investment banker.

Mansoor Raza Mirza, M.D. Dr. Mirza has served as a member of our board of directors since October 2010. He has also served as a scientific consultant to us since 2010. Dr. Mirza is Chief Oncologist at the Department of Oncology, Rigshospitalet the Copenhagen University Hospital, Denmark. Dr. Mirza is both a medical and radiation oncologist, with a primary focus in non-surgical treatment of gynecologic cancers. His key academic goals are to promote clinical research, international trial collaboration and education, and he has broad experience in clinical protocol development, trial conduct and clinical trial regulations. Dr. Mirza is the author of several phase 1, 2 and 3 studies and serves as the chair of the Independent Data Safety Monitoring Committee of the OUTBACK trial, which is a large international cervical cancer trial. He is the senior author of national Danish guidelines for the management of endometrial, cervical, vulvar and non-epithelial ovarian cancers as well as of NSGO radio therapy guidelines for cervical and vulvar cancers. His other current appointments include service as President-Elect of the Nordic Society of Gynecologic Oncology (NSGO), Medical Director of the NSGO-Clinical Trial Unit, Vice-Chairman of the Danish Gynecological Cancer Society, Founding Executive Member of the European Network of Gynecologic Oncology Trials Group, and membership on the faculty of the European Society of Medical Oncology. He also serves on the board of directors of the Gynecologic Cancer Intergroup, a private organization promoting high quality clinical trials, and Metamark Genetics Inc., a private biopharmaceutical company. He holds a M.D., Diploma in Surgery and Diploma in Clinical Oncology from the Pirogov Moscow State Medical Institute as well as post-graduate education and certification in radiation and medical oncology from the University of Southern Denmark. We believe Dr. Mirza's qualifications to serve on our board of directors include his position as an expert in the non-surgical treatment of cancer, and gynecologic cancers in particular, and his knowledge of our company and its business through service on our board since October 2010.

Kenneth E. Weg. Mr. Weg has served as a member of our board of directors since February 2013. He has over 34 years of experience in the pharmaceutical industry with global biopharmaceutical companies Bristol-Myers Squibb Company and Merck & Co., Inc. From 1993 to 1998, he was President, Worldwide Medicines Group of Bristol-Myers Squibb, responsible for all ethical pharmaceuticals and over-the-counter medicines on a global basis. Mr. Weg also served as Vice-Chairman of the Board of Bristol-Myers Squibb from 1993 to 1998. He retired from Bristol-Myers Squibb in February 2001. From January 2002 to August 2013, Mr. Weg served as a director of AVEO Pharmaceuticals, Inc., a public biotechnology company. Mr. Weg also served as non-Executive Chairman of Millennium Pharmaceuticals until that company was acquired by Takeda, Inc. in 2008. In addition, he has served as founder and Chairman of Metamark Genetics Inc., a private biotechnology company, since 2005. He holds a B.A. in English Literature from Dartmouth College and an M.B.A. from Columbia University. We believe Mr. Weg's qualifications to serve on our board of directors include his extensive leadership experience in the global pharmaceutical industry, including his extensive executive leadership at Bristol-Myers Squibb, and his experience as a member of the boards of directors of multiple biopharmaceutical companies.

Board Composition

Our board of directors is currently authorized to have nine members. Our board of directors currently consists of six directors, and there are three vacancies on our board. In accordance with the terms of our certificate of incorporation and bylaws, our board of directors is divided into three classes,

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class I, class II and class III, with members of each class serving staggered three-year terms. The members of the classes are divided as follows:

the class I directors are Mr. Greene and Dr. Mirza, and their term expires at the annual meeting of stockholders to be held in 2014;

the class II directors are Dr. Pakianathan and Mr. Weg, and their term expires at the annual meeting of stockholders to be held in 2015; and

the class III directors are Mr. Bohlin and Dr. Kauffman, and their term expires at the annual meeting of stockholders to be held in 2016.

Upon the expiration of the term of a class of directors, directors in that class will be eligible to be elected for a new three-year term at the annual meeting of stockholders in the year in which their term expires. Our directors may be removed only for cause by the affirmative vote of the holders of 75% or more of our stock entitled to vote thereon.

We have no formal policy regarding board diversity. Our priority in selection of board members is identification of members who will further the interests of our stockholders through his or her established record of professional accomplishment, the ability to contribute positively to the collaborative culture among board members, knowledge of our business and understanding of the competitive landscape.

Director Independence

The NASDAQ Listing Rules requires a majority of a listed company's board of directors to be comprised of independent directors within one year of listing. In addition, the NASDAQ Listing Rules require that, subject to specified exceptions, each member of a listed company's audit, compensation and nominating and corporate governance committees be independent and that audit committee members also satisfy independence criteria set forth in Rule 10A-3 under the Securities Exchange Act of 1934, as amended, or the Exchange Act.

Under the NASDAQ Listing Rules, a director will only qualify as an independent director if, in the opinion of our board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. Our board of directors has determined that each of our directors, with the exception of Dr. Kauffman and Dr. Mirza, is an independent director as defined under the NASDAQ Listing Rules. Our board of directors also determined that Mr. Bohlin, Mr. Greene and Dr. Pakianathan, who comprise our audit committee, Mr. Greene, Dr. Pakianathan and Mr. Weg, who comprise our compensation committee, and Mr. Bohlin and Mr. Weg, who are two of the members of our nominating and corporate governance committee, satisfy the independence standards for such committees established by the SEC and the NASDAQ Listing Rules, as applicable. In making such determinations, our board of directors considered the relationships that each such non-employee director has with our company and all other facts and circumstances our board of directors deemed relevant in determining independence, including the beneficial ownership of our capital stock by each non-employee director. Dr. Kauffman does not qualify as an independent director under the standards established by the SEC and the NASDAQ Listing Rules, but is a member of our nominating and corporate governance committee, under applicable exemptions in the NASDAQ Listing Rules. Under such exemptions, Dr. Kauffman is permitted to serve on the nominating and corporate governance committee for up to one year following the consummation of our initial public offering.

There are no family relationships among any of our directors or executive officers, except that Michael Kauffman, M.D., Ph.D., our Chief Executive Officer and a director, is married to Sharon Shacham, Ph.D., M.B.A., our President and Chief Scientific Officer.

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Board Committees

Our board has established three standing committees – audit, compensation, and nominating and corporate governance – each of which operates under a charter that has been approved by our board. We post current copies of each committee's charter on the Corporate Governance section of our website, www.karyopharm.com.

Audit Committee

The members of our audit committee are Mr. Bohlin, Mr. Greene and Dr. Pakianathan. Mr. Bohlin is the chair of the audit committee. Our board of directors has determined that Mr. Bohlin qualifies as an audit committee financial expert within the meaning of SEC rules. In making this determination, our board has considered the formal education and nature and scope of his previous experience, coupled with past and present service on various audit committees. Our audit committee assists our board of directors in its oversight of our accounting and financial reporting process and the audits of our financial statements. Our audit committee's responsibilities include:

- appointing, approving the compensation of, and assessing the independence of, our registered public accounting firm;
- overseeing the work of our registered public accounting firm, including through the receipt and consideration of reports from such firm;
- reviewing and discussing with management and the registered public accounting firm our annual and quarterly financial statements and related disclosures;
- monitoring our internal control over financial reporting, disclosure controls and procedures and code of business conduct and ethics;
- overseeing our internal audit function;
- discussing our risk management policies;
- establishing policies regarding hiring employees from the registered public accounting firm and procedures for the receipt and retention of accounting-related complaints and concerns;
- meeting independently with our internal auditing staff, registered public accounting firm and management;
- reviewing and approving or ratifying any related person transactions; and
- preparing the audit committee report required by SEC rules.

Compensation Committee

The members of our compensation committee are Mr. Greene, Dr. Pakianathan and Mr. Weg. Mr. Greene is the chair of the compensation committee. Our compensation committee assists our board of directors in the discharge of its responsibilities relating to the compensation of our executive officers. The compensation committee's responsibilities include:

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annually reviewing and approving corporate goals and objectives relevant to the compensation of our chief executive officer;

reviewing and approving, or making recommendations to our board with respect to, the compensation of our chief executive officer and our other executive officers;

overseeing an evaluation of our senior executives;

overseeing and administering our cash and equity incentive plans;

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reviewing and making recommendations to our board with respect to director compensation; and

reviewing and discussing annually with management our compensation disclosure required by SEC rules.

Nominating and Corporate Governance Committee

The members of our nominating and corporate governance committee are Mr. Bohlin, Dr. Kauffman and Mr. Weg. Mr. Weg is the chair of the nominating and corporate governance committee. The nominating and corporate governance committee's responsibilities include:

identifying individuals qualified to become board members;

recommending to our board the persons to be nominated for election as directors and to each of the board's committees;

reviewing and making recommendations to the board with respect to management succession planning;

developing and recommending to the board corporate governance principles; and

overseeing periodic evaluations of the board.

Compensation Committee Interlocks and Insider Participation

During 2013, the members of our compensation committee were Mr. Greene, Dr. Pakianathan and Mr. Weg. None of our executive officers served as a director or a member of a compensation committee (or other committee serving an equivalent function) of any other entity, one of whose executive officers served as a director or member of our compensation committee during the fiscal year ended December 31, 2013. During 2013, no member of our compensation committee was a current or former officer or employee of Karyopharm or had any related person transaction involving Karyopharm.

Code of Ethics and Code of Conduct

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. We have posted on our website, www.karyopharm.com, a current copy of the code and all disclosures that are required by law or NASDAQ stock market listing standards concerning any amendments to, or waivers from, any provision of the code.

Table of Contents**EXECUTIVE COMPENSATION**

This section discusses the material elements of our executive compensation policies and important factors relevant to an analysis of these policies. It provides qualitative information regarding the manner and context in which compensation is awarded to and earned by our executive officers named in the "Summary Compensation Table" below and is intended to place in perspective the information presented in the following tables and the corresponding narrative.

Summary Compensation Table

The following table sets forth information regarding compensation earned by each of our named executive officers during each of the fiscal years ending December 31, 2012 and 2013. We refer to these executive officers as our named executive officers elsewhere in this prospectus.

Summary Compensation Table

Name and Principal Position	Year	Salary (\$)	Option Awards \$(1)	Non-Equity Incentive Plan Compensation \$(2)	All Other Compensation \$(3)	Total (\$)
Michael G. Kauffman, M.D., Ph.D. <i>Chief Executive Officer</i> (4)	2013	380,507	6,771,948	170,000	12,739	7,335,194
	2012	352,240		97,900	13,138	463,278
Sharon Shacham, Ph.D., M.B.A. <i>President and Chief Scientific Officer</i>	2013	380,507	6,771,948	129,342	14,288	7,296,065
	2012	300,000	5,460	138,800	12,060	456,320
Paul Brannelly <i>Senior Vice President, Finance and Administration</i> (5)	2013	160,505	1,702,879	117,960	4,614	1,985,958
	2012					
Alan T. Barber <i>Acting Chief Financial Officer</i> (6)	2013	144,950	28,928			173,878
	2012	205,600	7,695			213,295

- (1) Amounts represent the aggregate fair value amount computed as of the grant date of the option awards granted during 2012 and 2013 in accordance with FASB ASC Topic 718. Assumptions used in the calculation of these amounts are included in Note 9, Stock-based Compensation, of the notes to our consolidated financial statements.
- (2) Amounts represent awards to our named executive officers under our annual performance-based cash incentive program. See "Narrative Disclosure to Summary Compensation Table Annual Performance-based Cash Incentives" for a description of that program. Annual bonus compensation for 2012 was earned in 2012 and paid in 2012. Annual bonus compensation for 2013 was earned in 2013 and paid in 2013.
- (3) Amounts represent (i) the dollar value of life insurance premiums paid by us on behalf of our named executive officers and (ii) the amount we contributed to our 401(k) plan in respect of our named executive officers. In 2012, we paid \$810 and \$60 in life insurance premiums on behalf of Dr. Kauffman and Dr. Shacham, respectively, and we contributed \$12,328 and \$12,000 to our 401(k) plan in respect of Dr. Kauffman and Dr. Shacham, respectively. In 2013, we paid \$58, \$25 and \$25 in life insurance premiums on behalf of Dr. Kauffman, Dr. Shacham and Mr. Brannelly, respectively. Also in 2013, we contributed \$12,681, \$14,263 and \$4,589 to our 401(k) plan in respect of Dr. Kauffman, Dr. Shacham and Mr. Brannelly, respectively.

(4)

Dr. Kauffman also serves as a member of our board of directors but does not receive any compensation for his service as a director.

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- (5) Mr. Brannelly joined us in June 2013 as our Senior Vice President, Finance and Administration.
- (6) Mr. Barber, consultant with The Prestar Group, served as our Acting Chief Financial Officer, and performed customary duties of a chief financial officer for us until his resignation from such position on July 25, 2013.

Narrative Disclosure to Summary Compensation Table

Our compensation committee makes compensation decisions regarding our named executive officers or makes recommendations concerning executive compensation to our board of directors. In May 2013, our compensation committee engaged Arnosti Consulting, Inc., an independent compensation consultant, to provide comparative data on executive compensation practices in our industry and to advise on our executive compensation program generally. Although our board of directors and compensation committee consider the advice and recommendation of any independent compensation consultants as to our executive compensation program, the board of directors and compensation committee ultimately make their own decisions about these matters.

Base Salary

Base salaries are used to recognize the experience, skills, knowledge and responsibilities required of our named executive officers. Historically, base salaries for our named executive officers typically have been established through arm's length negotiation at the time the executive officer is appointed, taking into account the position for which the named executive officer is being considered and the named executive officer's qualifications, prior experience and prior salary. None of our named executive officers is currently party to an employment agreement or other service agreement that provides for automatic or scheduled increases in base salary. However, on an annual basis, our compensation committee reviews and evaluates the need for adjustment of the base salaries of each of our named executive officers, including our chief executive officer. Our chief executive officer provides input to our compensation committee with respect to the base salaries of our named executive officers other than our chief executive officer. In making decisions regarding salary increases, we may also draw upon the experience of members of our board of directors with other companies.

In 2012, we paid base salaries to Dr. Kauffman and Dr. Shacham of \$352,240 and \$300,000, respectively, and we paid aggregate consulting fees to Mr. Barber of \$205,600, which fees were paid on an hourly basis. In 2013, we paid base salaries to Dr. Kauffman, Dr. Shacham and Mr. Brannelly of \$380,507, \$380,507 and \$160,505, respectively, and we paid aggregate consulting fees to Mr. Barber of \$144,950, which fees were paid on an hourly basis. The base salaries for 2014 for each of Dr. Kauffman, Dr. Shacham and Mr. Brannelly are \$440,000, \$385,000 and \$285,000, respectively.

Annual Performance-based Cash Incentives

We have designed our annual performance-based cash incentive program to emphasize pay-for-performance, on corporate and individual levels, and to reward our named executive officers for the preceding year's performance. Subsequent to our initial public offering, each named executive officer has been eligible, at our compensation committee's discretion, to receive an annual performance-based cash incentive, which we refer to as an annual cash incentive, in an amount corresponding to a percentage of his or her base salary. The target amount of the annual cash incentive is determined, prior to the applicable fiscal year, by our compensation committee, based upon the accomplishment of certain objective corporate milestones for the applicable fiscal year, and the amount of the annual cash incentive paid to our named executive officers is determined by our compensation committee, upon a consideration of the level of achievement of these milestones and a subjective evaluation of individual performance. The final evaluation made by our compensation committee does

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not involve a predetermined mathematical formula. Our compensation committee has authority to adjust the incentive percentage each year in connection with its review of our and the named executive officer's performance. Prior to our initial public offering, the foregoing decisions related to annual cash incentives for named our executive officers were made by our board of directors, based upon the recommendation of the compensation committee.

For 2012, the objective factors contributing to corporate performance were based on (i) the achievement of clinical and regulatory milestones, including effectiveness in the U.S. of an IND and authorization of a clinical trial application in Europe and Canada for the oral administration of Selinexor, recruitment of patients for human clinical trials, initiation of a Phase 2b clinical trial to support regulatory approval of Verdinexor and demonstration of activity of our SINE compounds in certain indications, and (ii) the achievement of a financial milestone consisting of the receipt of non-dilutive funding during 2012. Based upon the company's achievement, on or before the company's projected timeframe, of effectiveness of an IND in the U.S. and authorization of a clinical trial application in Europe and Canada for the oral administration of Selinexor and the successful recruitment of patients for human clinical trials, the board of directors determined that the company overachieved its expectations regarding corporate performance during 2012. The board of directors approved annual cash incentives for Drs. Kauffman and Shacham upon consideration of these corporate achievements along with subjective factors related to each named executive officer's individual performance, responsibilities and then existing compensation levels.

For 2013, the objective factors contributing to corporate performance were based on (i) the achievement of multiple fundraising milestones, including the completion of the sale of our series B and series B-1 preferred stock and our initial public offering and (ii) the achievement of clinical milestones, including expansion of Phase I clinical trials of Selinexor, enrollment of patients in clinical trials, initiation of investigator sponsored trials of Selinexor, preparation for registration-directed trials in hematological malignancy indications and completion of a Phase 2b clinical trial of Verdinexor in pet dogs with newly-diagnosed or after first relapse lymphomas. Based upon these clinical achievements and the completion of the company's fundraising milestones, the compensation committee of the board of directors approved annual cash incentives for Drs. Kauffman and Shacham and Mr. Brannelly upon consideration of these corporate achievements of 85% of each named executive officer's respective target for 2013.

In 2012, we awarded cash incentives to Dr. Kauffman and Dr. Shacham in the amounts of \$97,900 and \$138,800, respectively. In 2013, we awarded cash incentives to Dr. Kauffman, Dr. Shacham and Mr. Brannelly in the amounts of \$170,000, \$129,342 and \$117,960, respectively. We did not award any cash incentives to Mr. Barber in 2012 or 2013.

Equity Incentive Awards

Our equity award program is the primary vehicle for offering long-term incentives to our named executive officers. While we do not currently have any equity ownership guidelines for our named executive officers, we believe that equity grants provide our named executive officers with a strong link to our long-term performance, create an ownership culture and help to align the interests of our named executive officers and our stockholders. We believe stock options provide meaningful incentives to our named executive officers to achieve increases in the value of our stock over time. In addition, the vesting feature of our equity grants contributes to executive retention by providing an incentive to our named executive officers to remain employed by us during the vesting period.

Prior to our initial public offering, our named executive officers were eligible to participate in the 2010 Stock Incentive Plan, as amended, or the 2010 Plan. Prior to our initial public offering, all stock options granted to our named executive officers were granted pursuant to the 2010 Plan. Following the closing of our initial public offering, our named executive officers and employees became

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eligible to receive stock options and other stock-based awards pursuant to the 2013 Stock Incentive Plan, or the 2013 Plan. Subsequent to our initial public offering, all stock options granted to our named executive officers have been granted pursuant to the 2013 Plan.

We have used stock options to compensate our named executive officers in the form of initial grants in connection with the named executive officer's appointment to his or her position, generally on an annual basis thereafter, and also at various times, including, prior to our initial public offering, concurrent with our preferred stock financings in order to address dilution to existing options attributable to such financings. Prior to our initial public offering, the award of stock options to our named executive officers has been made upon the recommendation of the compensation committee and the approval of our board of directors. Subsequent to our initial public offering, such awards have been made upon the approval of our compensation committee. None of our named executive officers is currently party to an employment or other service agreement with us that provides for automatic award of stock options. We have granted stock options to our named executive officers with time-based vesting, and, prior to our initial public offering, with performance-based vesting and an ability to early exercise. The options that we grant to our named executive officers with time-based vesting typically become exercisable as to 25% of the shares underlying the option on the first anniversary of the grant date, and as to an additional 1/48th of the shares underlying the option on a monthly basis thereafter. The options that we have granted to our named executive officers with performance-based vesting become exercisable upon the attainment of certain operational milestone events recommended by the compensation committee and approved by our board of directors. The options that we have granted to our named executive officers with an ability to early exercise are immediately exercisable in full, provided that any shares issued upon exercise will remain subject to the original vesting terms. In addition, such shares that are vested or unvested are subject to repurchase by us in the event such named executive officer ceases service to us or our successor in the capacity of an employee, officer, director or consultant for cause. Unvested shares are subject to repurchase by us in the event such named executive officer ceases service to us or our successor, other than for cause. For all options, vesting rights cease upon, and exercise rights cease shortly after, termination of employment or other service except in the case of death or disability. Prior to the exercise of an option, the holder has no rights as a stockholder with respect to the shares subject to such option, including no voting rights and no right to receive dividends or dividend equivalents.

In November 2010, we issued awards of restricted stock pursuant to the 2010 Plan, which we refer to as founders shares, to compensate Dr. Kauffman and Dr. Shacham in connection with their service to us from inception to such date and their expected continued service following such date. The founders shares vested as to 25% of the shares underlying the awards upon the first sale of shares of our series A preferred stock in October 2010, and vest as to an additional 1/48th of the shares underlying the awards on a monthly basis thereafter. These founders shares became fully vested in October 2013.

In 2013, prior to our initial public offering, our board of directors granted stock options to our named executive officers, pursuant to our 2010 Plan, as follows:

Name	Date of Grant	Option Award (#)	Grant Date
			Fair Value \$(1)
Michael G. Kauffman, M.D., Ph.D.	9/3/2013	480,303	4,228,083
Sharon Shacham, Ph.D., M.B.A.	9/3/2013	480,303	4,228,083
Paul Brannelly	9/3/2013	56,061	493,502
	7/25/2013	63,636	373,536
Alan T. Barber	7/25/2013	4,545	28,928

- (1) Amounts listed represent the aggregate fair value amount computed as of the grant date of the option awards granted in accordance with FASB ASC Topic 718. Assumptions used in the calculation of these amounts are included in Note 9, Stock-based Compensation, of the notes to our consolidated financial statements.

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In 2013, subsequent to our initial public offering, our compensation committee granted stock options to our named executive officers, pursuant to our 2013 Plan, as follows:

Name	Date of Grant	Option Award (#)	Grant Date
			Fair Value \$(1)
Michael G. Kauffman, M.D., Ph.D.	12/18/2013	140,000	2,543,865
Sharon Shacham, Ph.D., M.B.A.	12/18/2013	140,000	2,543,865
Paul Brannelly	12/18/2013	46,000	835,841

- (1) Amounts listed represent the aggregate fair value amount computed as of the grant date of the option awards granted in accordance with FASB ASC Topic 718.

2013 Outstanding Equity Awards at Fiscal Year-End

The following table sets forth information concerning outstanding equity awards for each of our named executive officers at December 31, 2013:

Name	Option Awards				Stock Awards	
	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price (\$)	Option Expiration Date	Number of Shares or Units of Stock That Have Not Vested (#)	Market Value of Shares or Units of Stock That Have Not Vested(1) (\$)
Michael G. Kauffman, M.D., Ph.D.	21,212	21,212(2)	\$ 0.26	12/14/2021		
	12,500	20,833(3)	\$ 0.26	12/14/2021		
		480,303(4)	\$ 4.75	9/2/2023		
		140,000(5)	\$ 23.66	12/17/2023		
					93,370(6)	2,140,040
Sharon Shacham, Ph.D., M.B.A.	39,748		\$ 0.03	10/21/2020		
	71,449(6)		\$ 0.03	10/21/2020		
	18,657(7)	4,910	\$ 0.03	11/1/2020		
	19,696	19,698(8)	\$ 0.26	12/14/2021		
	11,363	18,940(9)	\$ 0.26	12/14/2021		
		480,303(4)	\$ 4.75	9/2/2023		
Paul Brannelly		140,000(5)	\$ 23.66	12/17/2023		
					63,636	1,458,537
		56,061(4)	\$ 4.75	9/2/2023		
Alan T. Barber		46,000(5)	\$ 23.66	12/17/2023		
	3,535	2,526(11)	\$ 0.26	8/1/2021		
	568	947(12)	\$ 0.26	12/14/2021		
	757	2,273(13)	\$ 1.49	12/6/2022		
	3,030	1,515(14)	\$ 4.75	7/24/2023		

- (1) Represents the market value of the shares based on the closing price on December 31, 2013 of \$22.92 per share.

- (2) The unvested awards are scheduled to vest in equal monthly installments through December 1, 2015.

- (3)

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The unvested awards are scheduled to vest in equal monthly installments through June 1, 2016.

- (4) The option vests as to 25% of the shares on September 3, 2014 and thereafter in 36 equal monthly installments.
- (5) The option vests as to 25% of the shares on December 18, 2014 and thereafter in 36 equal monthly installments.

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- (6) The option is subject to an early exercise provision and is immediately exercisable in full, provided that any shares issued upon exercise of such option will remain subject to the original vesting terms of such option and subject to repurchase by us in certain circumstances. As of December 31, 2013, 71,449 shares were vested.
- (7) The option is subject to an early exercise provision and is immediately exercisable in full, provided that any shares issued upon exercise of such option will remain subject to the original vesting terms of such option and subject to repurchase by us in certain circumstances. As of December 31, 2013, 18,657 shares were vested and 4,910 unvested shares underlying the option are scheduled to vest in equal monthly installments through October 1, 2014.
- (8) The unvested awards are scheduled to vest in equal monthly installments through December 1, 2015.
- (9) The unvested awards are scheduled to vest in equal monthly installments through June 1, 2016.
- (10) The award vests as to 25% of the shares on June 1, 2014 and thereafter in equal monthly installments.
- (11) The unvested awards are scheduled to vest in equal monthly installments through August 1, 2015.
- (12) The unvested awards are scheduled to vest in equal monthly installments through June 1, 2016.
- (13) The unvested awards are scheduled to vest in equal monthly installments through December 1, 2016.
- (14) The option vests in 6 equal monthly installments.

Employment Agreements, Severance and Change in Control Arrangements

We expect to enter into new employment agreements with each of our named executive officers to ensure that overall compensation for each named executive officer provides appropriate retention and performance incentives based in part on the recommendations of our compensation consultant and all subject to the review and approval of our compensation committee.

Historically, we have entered into employment agreements with each of our named executive officers, except for Mr. Barber, pursuant to which such named executive officers are employed "at will," meaning the executive or we may terminate the employment arrangement at any time. Such employment agreements establish the named executive officer's title, initial compensation arrangements, eligibility for benefits made available to employees generally and also provide for certain benefits upon termination of employment under specified conditions. The following summarizes such termination benefits under our named executive officers' existing employment agreements.

Benefits Provided Upon Termination Without Cause or for Good Reason Upon a Change in Control

Under the terms of the existing employment agreements we have entered into with each of Dr. Kauffman and Dr. Shacham, subject to the execution and effectiveness of a separation agreement that includes a release of claims against us, if such executive's employment is terminated by us without cause or by such executive for good reason, as defined in such employment agreements, after a change of control, as defined in such employment agreements, we will be obligated to pay (i) in the case of Dr. Kauffman, an amount equal to his then-current base salary for a period of eight months, or, in the case of Dr. Shacham, an amount equal to her then-current base salary for a period of six months, (ii) any earned but unpaid annual cash incentive and (iii) all other payments and benefits to which the executive was entitled on such date of termination under the terms of any applicable arrangement, plan or program in effect at the time of such termination.

We entered into a consulting agreement with Mr. Barber regarding his service to us as an independent contractor, which does not provide Mr. Barber with any employee benefits or any benefits upon termination of his service relationship with us.

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Non-Disclosure Agreements

We have entered into non-disclosure and inventions assignment agreements with Dr. Kauffman, Dr. Shacham and Mr. Brannelly and have entered into a consulting agreement with Mr. Barber which governs inventions assignment and confidential and proprietary information non-disclosure. Under the non-disclosure and inventions assignment agreements, Dr. Kauffman, Dr. Shacham and Mr. Brannelly have agreed (i) not to compete with us during his or her employment and for a period of twelve months after the termination of his or her employment; (ii) not to solicit our employees or customers during his or her employment and for a period of twelve months after the termination of his or her employment; (iii) to protect our confidential and proprietary information, and (iv) to assign to us related intellectual property that is developed during the course of his or her employment. Under the consulting agreement, Mr. Barber has agreed (i) not to solicit our employees during his service to us and for a period of twelve months after the termination of his service relationship with us; (ii) to protect our confidential and proprietary information and (iii) to assign to us related intellectual property that is developed during the course of his service to us.

Equity and Non-Equity Incentive Plans

2013 Stock Incentive Plan

Our board of directors adopted, and our stockholders approved, the 2013 stock incentive plan, which we refer to as the 2013 Plan, which became effective immediately prior to the closing of our initial public offering. The 2013 Plan provides for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock unit awards, and other stock-based awards. As of February 28, 2014, 2,358,217 shares of our common stock are reserved for issuance under the 2013 Plan. Additional shares of our common stock may also become available for issuance under the 2013 Plan. The number of such additional shares is equal to the sum of (1) the number of shares of our common stock subject to outstanding awards under our 2010 Plan that expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by us at their original issuance price pursuant to a contractual repurchase right and (2) an annual increase to be added on the first day of each fiscal year, until, and including, the fiscal year ending December 31, 2023, equal to the least of (A) 1,939,393 shares of our common stock, (B) 4% of the number of shares of our common stock outstanding on the first day of the fiscal year, and (C) an amount determined by our board of directors.

Our employees, officers, directors, consultants, and advisors, and employees, officers, directors, consultants, and advisors of any of our present or future parent or subsidiary corporations and any other business venture (including, without limitation, joint venture or limited liability company) in which we have a controlling interest, as determined by our board of directors, are eligible to be granted awards under the 2013 Plan. However, incentive stock options may only be granted to employees who are eligible to receive incentive stock options under the Internal Revenue Code.

The 2013 Plan is administered by our board of directors or a committee or officer appointed by our board of directors. Pursuant to the terms of the 2013 Plan, our board of directors or such committee or officer (subject to the below) selects the recipients of awards and determines:

the number of shares of our common stock covered by options and the conditions and limitations applicable to the exercise of options;

the type of options to be granted;

the duration of options, which may not be in excess of ten years;

the exercise price of options, which must be at least equal to the fair market value of our common stock on the date of grant; and

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the number of shares of our common stock subject to any stock appreciation rights, restricted stock awards, restricted stock unit awards, or other stock-based awards and the terms and conditions of such awards, including conditions for vesting and repurchase (or forfeiture), issue price and repurchase price (provided that the measurement price of stock appreciation rights must be at least equal to the fair market value of our common stock on the date of grant and the duration of stock appreciation rights may not be in excess of ten years).

Our board of directors has delegated its powers under the 2013 Plan to our compensation committee. If our board of directors delegates authority to an officer to grant awards under the 2013 Plan, the officer will have the power to grant awards to all of our employees, except executive officers. Our board of directors will fix the terms of awards to be granted by such officer, including the exercise price of such awards (which may include a formula by which the exercise price will be determined) and the maximum number of shares subject to awards that the officer may grant.

In the event of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification of shares, spin-off or other similar change in capitalization or event, or any dividend or distribution to holders of our common stock other than an ordinary cash dividend, our board of directors is required by the 2013 Plan to make equitable adjustments, in a manner determined by our board, to:

the number and class of securities available under, and the share counting rules set forth in, the 2013 Plan;

the number and class of securities and exercise price per share of each outstanding option;

the share and per-share provisions and measurement price of each outstanding stock appreciation right;

the number of shares and the repurchase price per share subject to each outstanding restricted stock award or restricted stock unit award; and

the share and per-share-related provisions and purchase price, if any, of any other outstanding stock-based award.

In connection with a merger or other reorganization event (as defined in the 2013 Plan), our board of directors may take any one or more of the following actions as to all or any portion of any outstanding awards other than restricted stock, on such terms as it determines:

provide that all outstanding awards shall be assumed, or substantially equivalent awards shall be substituted, by the acquiring or succeeding corporation (or an affiliate thereof);

upon written notice to a participant, provide that all of the participant's unvested and/or unexercised awards will terminate immediately prior to the consummation of such reorganization event unless exercised by the participant (to the extent then exercisable) within a specified period following the date of such notice;

in the event of a reorganization event pursuant to which holders of shares of our common stock will receive a cash payment for each share surrendered in the reorganization event, make or provide for a cash payment to participants with respect to each award held by a participant equal to (1) the number of shares of our common stock subject to the vested portion of the award (after giving effect to any acceleration of vesting that occurs upon or immediately prior to such reorganization event) multiplied by (2) the excess, if any, of the cash payment for each share surrendered in the reorganization event over the exercise, measurement or purchase price of such award and any applicable tax withholdings, in exchange for termination of such award; and/or

provide that in connection with our liquidation or dissolution, awards shall convert into the right to receive liquidation proceeds (if applicable, net of the exercise, measurement or purchase price thereof and any applicable tax withholdings).

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Our board of directors is not obligated under the 2013 Plan to treat all awards, all awards held by a participant, or all awards of the same type, identically in connection with a reorganization event.

In the case of certain restricted stock unit awards, no assumption or substitution will be permitted and the restricted stock unit awards will instead be settled in accordance with the terms of the applicable restricted stock unit agreement, and in certain circumstances, any unvested restricted stock unit awards will be terminated immediately prior to the consummation of the reorganization event without any payment in exchange therefor.

Upon the occurrence of a reorganization event other than our liquidation or dissolution, the repurchase and other rights with respect to outstanding awards of restricted stock will continue for the benefit of the successor company and will, unless our board of directors otherwise determines, apply to the cash, securities or other property into which our common stock was converted into or exchanged for pursuant to the reorganization event in the same manner and to the same extent as they applied to such restricted stock. Upon the occurrence of a reorganization event involving our liquidation or dissolution, all restrictions and conditions on all restricted stock then outstanding will automatically be deemed terminated or satisfied, unless otherwise provided in the instrument evidencing the award of restricted stock or any other agreement between a participant and us.

At any time, our board of directors may provide that any award under the 2013 Plan shall become immediately exercisable in whole or in part, free of some or all restrictions or conditions, or otherwise realizable in whole or in part, as the case may be.

In addition, the 2013 Plan provides that, notwithstanding the provisions of the plan that may apply upon a reorganization event and except as otherwise provided for in the instrument evidencing an option or award of restricted stock or any other agreement between us and the participant, upon the occurrence of a change in control event (as defined in the 2013 Plan) each option shall become immediately exercisable and each award of restricted stock shall become immediately free from all conditions and restrictions, if, in either case, the employment of the participant holding such award is terminated by us (or our acquiring or succeeding corporation) without cause (as defined in the 2013 Plan) or by the participant for good reason (as defined in the 2013 Plan), on or prior to the first anniversary of the date of the change in control event. Our board of directors may specify in an award at the time of grant the effect of a change in control event on any stock appreciation right, restricted stock unit or other stock-based award.

Except with respect to certain actions requiring stockholder approval under the Internal Revenue Code or the rules of the NASDAQ Stock Market, our board of directors may amend, modify or terminate any outstanding award under the 2013 Plan, including but not limited to, substituting therefor another award of the same or a different type, changing the date of exercise or realization, and converting an incentive stock option into a non-qualified stock option, subject to certain participant consent requirements. Unless our stockholders approve such action, the 2013 Plan provides that we may not (except as otherwise permitted in connection with a change in capitalization or reorganization event):

amend any outstanding stock option or stock appreciation right granted under the 2013 Plan to provide an exercise or measurement price per share that is lower than the then-current exercise or measurement price per share of such outstanding award;

cancel any outstanding option or stock appreciation right (whether or not granted under the 2013 Plan) and grant in substitution therefor new awards under the 2013 Plan (other than substitute awards permitted in connection with a merger or consolidation of an entity with us or our acquisition of property or stock of another entity) covering the same or a different number of shares of our common stock and having an exercise or measurement price per

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share lower than the then-current exercise or measurement price per share of the cancelled award;

cancel in exchange for a cash payment any outstanding option or stock appreciation right with an exercise or measurement price per share above the then-current fair market value of our common stock; or

take any other action that constitutes a "repricing" within the meaning of the rules of the NASDAQ Stock Market.

No award may be granted under the 2013 Plan after October 21, 2023, but awards previously granted may extend beyond that date. Our board of directors may amend, suspend or terminate the 2013 Plan or any portion thereof at any time, subject to certain stockholder approval requirements and limitations under the Internal Revenue Code.

2013 Employee Stock Purchase Plan

Our board of directors adopted, and our stockholders approved, the 2013 Employee Stock Purchase Plan, or the 2013 ESPP. The 2013 ESPP is administered by our board of directors or by a committee appointed by our board of directors. The 2013 ESPP provides participating employees with the opportunity to purchase an aggregate of 242,424 shares of our common stock. The number of shares of our common stock reserved for issuance under the 2013 ESPP will automatically increase on the first day of each fiscal year, commencing on January 1, 2015 and ending on December 31, 2023, in an amount equal to the least of (1) 484,848 shares of our common stock, (2) 1% of the total number of shares of our common stock outstanding on the first day of the applicable year, and (3) an amount determined by our board of directors.

All of our employees and employees of any of our designated subsidiaries, as defined in the 2013 ESPP, are eligible to participate in the 2013 ESPP, provided that:

such person is customarily employed by us or a designated subsidiary for more than 20 hours a week and for more than five months in a calendar year;

such person has been employed by us or by a designated subsidiary for at least 30 days prior to enrolling in the 2013 ESPP; and

such person was our employee or an employee of a designated subsidiary on the first day of the applicable offering period under the 2013 ESPP.

No employee may purchase shares of our common stock under the 2013 ESPP and any of our other employee stock purchase plans in excess of \$25,000 of the fair market value of our common stock (as of the date of the option grant) in any calendar year. In addition, no employee may purchase shares of our common stock under the 2013 ESPP that would result in the employee owning 5% or more of the total combined voting power or value of our stock.

We expect to make one or more offerings to our eligible employees to purchase stock under the 2013 ESPP beginning at such time as our board of directors may determine. Each offering will consist of a six-month offering period during which payroll deductions will be made and held for the purchase of our common stock at the end of the offering period. Our board of directors may, at its discretion, choose a different period of not more than 12 months for offerings. Our board of directors has determined that the first six-month offering period under the 2013 ESPP will begin on May 1, 2014.

On the commencement date of each offering period, each eligible employee may authorize up to a maximum of 15% of his or her compensation to be deducted by us during the offering period. Each employee who continues to be a participant in the 2013 ESPP on the last business day of the offering period will be deemed to have exercised an option to purchase from us the number of whole

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shares of our common stock that his or her accumulated payroll deductions on such date will pay for, not in excess of the maximum numbers set forth above. Under the terms of the 2013 ESPP, the purchase price shall be determined by our board of directors for each offering period and will be at least 85% of the applicable closing price of our common stock. If our board of directors does not make a determination of the purchase price, the purchase price will be 85% of the lesser of the closing price of our common stock on the first business day of the offering period or on the last business day of the offering period.

An employee may for any reason withdraw from participation in an offering prior to the end of an offering period and permanently draw out the balance accumulated in the employee's account. If an employee elects to discontinue his or her payroll deductions during an offering period but does not elect to withdraw his or her funds, funds previously deducted will be applied to the purchase of common stock at the end of the offering period. If a participating employee's employment ends before the last business day of an offering period, no additional payroll deductions will be made and the balance in the employee's account will be paid to the employee.

We will be required to make equitable adjustments to the number and class of securities available under the 2013 ESPP, the share limitations under the 2013 ESPP, and the purchase price for an offering period under the 2013 ESPP to reflect stock splits, reverse stock splits, stock dividends, recapitalizations, combinations of shares, reclassifications of shares, spin-offs and other similar changes in capitalization or events or any dividends or distributions to holders of our common stock other than ordinary cash dividends.

In connection with a merger or other reorganization event (as defined in the 2013 ESPP), our board of directors or a committee of our board of directors may take any one or more of the following actions as to outstanding options to purchase shares of our common stock under the 2013 ESPP on such terms as our board or committee determines:

provide that options shall be assumed, or substantially equivalent options shall be substituted, by the acquiring or succeeding corporation (or an affiliate thereof);

upon written notice to employees, provide that all outstanding options will be terminated immediately prior to the consummation of such reorganization event and that all such outstanding options will become exercisable to the extent of accumulated payroll deductions as of a date specified by our board or committee in such notice, which date shall not be less than ten days preceding the effective date of the reorganization event;

upon written notice to employees, provide that all outstanding options will be cancelled as of a date prior to the effective date of the reorganization event and that all accumulated payroll deductions will be returned to participating employees on such date;

in the event of a reorganization event under the terms of which holders of our common stock will receive upon consummation thereof a cash payment for each share surrendered in the reorganization event, change the last day of the offering period to be the date of the consummation of the reorganization event and make or provide for a cash payment to each employee equal to (1) the cash payment for each share surrendered in the reorganization event times the number of shares of our common stock that the employee's accumulated payroll deductions as of immediately prior to the reorganization event could purchase at the applicable purchase price, where the acquisition price is treated as the fair market value of our common stock on the last day of the applicable offering period for purposes of determining the purchase price and where the number of shares that could be purchased is subject to the applicable limitations under the 2013 ESPP minus (2) the result of multiplying such number of shares by the purchase price; and/or

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provide that, in connection with our liquidation or dissolution, options shall convert into the right to receive liquidation proceeds (net of the purchase price thereof).

Our board of directors may at any time, and from time to time, amend or suspend the 2013 ESPP or any portion thereof. We will obtain stockholder approval for any amendment if such approval is required by Section 423 of the Internal Revenue Code. Further, our board of directors may not make any amendment that would cause the 2013 ESPP to fail to comply with Section 423 of the Internal Revenue Code. The 2013 ESPP may be terminated at any time by our board of directors. Upon termination, we will refund all amounts in the accounts of participating employees.

2010 Stock Incentive Plan

In July 2013, our board of directors adopted and our stockholders approved the amended and restated 2010 stock incentive plan, which we refer to as the 2010 Plan. The 2010 Plan provides for the grant of incentive stock options, nonstatutory stock options, restricted stock awards, restricted stock unit awards, and other stock-based awards. We no longer grant awards under the 2010 Plan, but awards remain outstanding under the 2010 Plan in accordance with their terms.

The 2010 Plan is administered by our board of directors. Pursuant to the terms of the 2010 Plan, our board of directors selected the recipients of awards and determined:

the number of shares of our common stock covered by options;

the terms, conditions and limitations applicable to the grant or exercise of options and to the common stock to be issued upon exercise of each option, including vesting provisions, repurchase provisions and restrictions upon sale or transfer thereof;

the type of options to be granted;

the vesting and duration of options;

the exercise price of options; and

the number of shares of our common stock subject to and the terms and conditions of any restricted stock awards, restricted stock unit awards, or other stock-based awards, including conditions for repurchase (or forfeiture) and repurchase price.

To the extent permitted by applicable law, our board of directors may delegate its powers under the 2010 Plan to one or more committees or subcommittees of our board or to one or more of our executive officers.

In the event of any stock split, reverse stock split, stock dividend, recapitalization, combination or reclassification of shares, spin-off or other similar change in capitalization or event, we are required by the 2010 Plan to make appropriate adjustments, in a manner determined by our board, to:

the number and class of securities available and the per-participant share limits under the 2010 Plan;

the number and class of securities, vesting schedule, and exercise price per share of each outstanding award;

the repurchase price per security subject to repurchase; and

the terms of each other outstanding stock-based award.

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Upon the consummation of a merger or other event constituting an acquisition (as defined in the 2010 Plan), our board of directors or the board of directors of the surviving or acquiring entity shall, as to outstanding awards under the 2010 Plan (on the same basis or on different bases), either:

make appropriate provision for the continuation or assumption of such awards or substitute on an equitable basis for the shares then subject to such awards either (1) the consideration payable with respect to the outstanding shares of our common stock in connection with the acquisition, (2) shares of stock of the surviving or acquiring corporation, or (3) such other securities or other consideration as the applicable board deems appropriate, the fair market value of which shall not materially differ from the fair market value of the shares of our common stock subject to such awards immediately preceding the acquisition;

upon written notice, provide that one or more awards then outstanding must be exercised (to the extent then vested), in whole or in part, within a specified number of days of the date of such notice, at the end of which period such awards shall terminate; or

provide that one or more awards then outstanding, in whole or in part, shall be terminated in exchange for a cash payment equal to the excess of the fair market value (as determined by the applicable board in its sole discretion) for the vested shares subject to such awards over the exercise price, if any, thereof.

Unless otherwise determined by the applicable board, any repurchase rights or other rights that relate to an award shall continue to apply to consideration, including cash, that has been substituted, assumed or amended for an award in connection with an acquisition. We may require that all or any portion of such consideration payable in respect of an award in connection with an acquisition shall be held in escrow (including in an escrow pursuant to the agreement effecting such acquisition) in order to effectuate any continuing restrictions.

At any time, our board of directors may provide that any award under the 2010 Plan shall become immediately exercisable in full or in part or free of some or all restrictions or conditions, or otherwise realizable in full or in part, as the case may be.

Our board of directors may amend, modify or terminate any outstanding award under the 2010 Plan, including, but not limited to, substituting therefor another award of the same or a different type, changing the date of exercise or realization, and converting an incentive stock option to a nonstatutory stock option, subject to certain participant consent requirements. In addition, our board of directors may, without stockholder approval, amend any outstanding option to reduce the exercise price of such option or cancel any outstanding option and grant in substitution therefor new options covering the same or a different number of shares of our common stock and having a lower exercise price than the cancelled options. Our board of directors may amend, suspend or terminate the 2010 Plan or any portion thereof at any time.

401(k) Retirement Plan

We maintain a 401(k) retirement plan that is intended to be a tax-qualified defined contribution plan under Section 401(k) of the Internal Revenue Code. In general, all of our U.S.-based employees are eligible to participate in the 401(k) plan, beginning on the first day of the month following commencement of their employment. The 401(k) plan includes a salary deferral arrangement pursuant to which participants may elect to reduce their current compensation by up to the statutorily prescribed limit, equal to \$17,500 in 2013, and have the amount of the reduction contributed to the 401(k) plan.

Table of Contents**2013 Director Compensation**

Our director compensation program is intended to provide a total compensation package that enables us to attract and retain qualified and experienced individuals to serve as directors and to align our directors' interests with those of our stockholders. The following table sets forth information concerning the total compensation for our non-employee directors during the fiscal year ended December 31, 2013:

Director Compensation

Name(1)	Fees Paid In Cash (\$)(2)	Option Awards (\$)(3)	All Other Compensation (\$)	Total (\$)
Garen G. Bohlin	10,357	109,075		119,432
Barry E. Greene	7,143	52,377		59,520
Deepa R. Pakianathan, Ph.D.	5,714	245,878		251,592
Mansoor Raza Mirza, M.D.	4,286	312,914	293,110(4)	610,310
Kenneth E. Weg	6,429	52,359		58,788

- (1) Dr. Kauffman, one of our directors who also serves as our Chief Executive Officer, does not receive any compensation for his service as a director.
- (2) Amounts represent cash compensation for services rendered by each member of our board of directors.
- (3) Amounts listed represent the aggregate fair value amount computed as of the grant date of the option awards granted during 2013 in accordance with FASB ASC Topic 718. Assumptions used in the calculation of these amounts are included in Note 9, Stock-based Compensation, of the notes to our consolidated financial statements.
- (4) Amount listed represents \$293,110 paid to Mirza Consulting, an entity wholly-owned by Dr. Mirza, for consulting and advisory services provided to us by Dr. Mirza other than for his service on the board of directors.

Prior to our initial public offering, the compensation of our non-employee directors was established through arm's length negotiation at the time the director was elected, taking into account the responsibilities of each director, such as committee service, and the director's qualifications and prior experience and industry data for such responsibilities. This compensation was reviewed and recommended by our compensation committee and approved by our board.

The stock options granted to our non-employee directors for service on our board have an exercise price equal to the fair market value of our common stock on the date of grant, expire ten years after the date of grant, and are subject to the director's continued service on our board. To the extent that a non-employee director has other responsibilities in addition to service on our board, such director may receive additional compensation to the extent as deemed appropriate by our board. Each member of our board of directors receives reimbursement for reasonable travel and other expenses incurred in connection with attending meetings of the board of directors, consistent with our travel expense reimbursement guidelines.

Dr. Mirza serves as a special scientific consultant to us pursuant to a consulting agreement with an entity wholly-owned by Dr. Mirza, for which he is paid (through such entity) a consulting fee of \$28,500 per month. See "Certain relationships and related person transactions Consulting Arrangements."

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Director Compensation Guidelines Following Our Initial Public Offering

On October 8, 2013, our board, upon the recommendation of our compensation committee, established the following compensation guidelines for non-employee directors, effective upon the closing of our initial public offering:

Each non-employee director will receive, on an annual basis, a cash retainer of \$30,000 and an option to purchase 10,000 shares of our common stock, which option shall vest in full on the first anniversary of the grant date;

Any non-employee director serving as independent chairman or lead independent director of the board will receive an additional cash retainer of \$20,000 per year;

Each non-employee director who serves as a chairperson of either of the audit committee or the compensation committee will receive a cash retainer of \$15,000 per year;

Each non-employee director who serves as a chairperson of the nominating and corporate governance committee will receive a cash retainer of \$10,000 per year;

Each non-employee director who serves on the audit committee, the compensation committee or the nominating and corporate governance committee will receive a cash retainer of \$5,000 per year for service on each such committee; and

Each non-employee director elected to the board following the closing of our initial public offering will receive a one-time award of an option to purchase 20,000 shares of our common stock, which option shall vest with respect to one-third of the shares on the first anniversary of the grant date and with respect to an additional one-thirty-sixth of the shares at the end of each successive month following the first anniversary of the grant date until the third anniversary of the grant date.

Limitation of Liability and Indemnification

Our certificate of incorporation limits the personal liability of directors for breach of fiduciary duty to the maximum extent permitted by the Delaware General Corporation Law and provides that no director will have personal liability to us or to our stockholders for monetary damages for breach of fiduciary duty as a director. However, these provisions do not eliminate or limit the liability of any of our directors:

for any breach of the director's duty of loyalty to us or our stockholders;

for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law;

for voting or assenting to unlawful payments of dividends, stock repurchases or other distributions; or

for any transaction from which the director derived an improper personal benefit.

Any amendment to or repeal of these provisions will not eliminate or reduce the effect of these provisions in respect of any act, omission or claim that occurred or arose prior to such amendment or repeal. If the Delaware General Corporation Law is amended to provide for further limitations on the personal liability of directors of corporations, then the personal liability of our directors will be further limited to the greatest extent permitted by the Delaware General Corporation Law.

In addition, our certificate of incorporation provides that we must indemnify our directors and officers and we must advance expenses, including attorneys' fees, to our directors and officers in connection with legal proceedings, subject to very limited exceptions.

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We maintain a liability insurance policy that covers certain liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers. In addition, we have entered into indemnification agreements with all of our directors. These indemnification agreements require us, among other things, to indemnify each such director for certain expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by him in any action or proceeding arising out of his service as one of our directors.

Certain of our non-employee directors may, through their relationships with their employers, be insured and/or indemnified against certain liabilities incurred in their capacity as members of our board of directors.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, executive officers or persons controlling us, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

Table of Contents**CERTAIN RELATIONSHIPS AND RELATED PERSON TRANSACTIONS**

Since January 1, 2011, we have engaged in the following transactions with our directors and executive officers and holders of more than 5% of our voting securities and affiliates of our directors, executive officers and such 5% stockholders. We believe that all of the transactions described below were made on terms no less favorable to us than could have been obtained from unaffiliated third parties.

Participation in Initial Public Offering

In our initial public offering, certain of our 5% stockholders and their affiliates purchased an aggregate of 625,000 shares of our common stock. Each of those purchases was made through the underwriters at the initial public offering price. The following table sets forth the aggregate number of shares of our common stock that these 5% stockholders and their affiliates purchased in our initial public offering:

Purchaser	Shares of Common Stock
Delphi Ventures and affiliates(1)	312,500
Foresite Capital Fund I, L.P.	312,500

(1)

Consists of 309,478 shares of common stock purchased by Delphi Ventures VIII, L.P. and 3,022 shares of common stock purchased by Delphi BioInvestments VIII, L.P. Deepa R. Pakianathan, Ph.D., a member of our board of directors, is a Managing Member of Delphi Management Partners VIII, L.L.C, the general partner of Delphi Ventures VIII, L.P. and Delphi BioInvestments VIII, L.P.

Preferred Stock Financings*Series B-1 Preferred Stock Financing*

In July 2013, we issued and sold an aggregate of 8,636,362 shares of our series B-1 preferred stock, at a purchase price per share of \$2.20, for an aggregate purchase price of \$18,999,996, and immediately following such sale, Foresite Capital, which purchased 6,818,182 shares of our series B-1 preferred stock in this financing, became a beneficial owner of more than 5% of our voting securities.

The following table sets forth the number of shares of series B-1 preferred stock that were issued to holders of more than 5% of our voting securities at the time of such issuance and affiliates of such holders, in connection with the series B-1 preferred stock financing and the aggregate cash purchase price paid by such entities.

Purchaser	Shares of Series B-1 Preferred Stock	Purchase Price
Delphi Ventures and affiliates(1)	909,091	\$ 2,000,000

(1)

Consists of 900,300 shares purchased by Delphi Ventures VIII, L.P. and 8,791 shares purchased by Delphi BioInvestments VIII, L.P.

Series B Preferred Stock Financing

Between April and September 2013, we issued and sold an aggregate of 24,100,000 shares of our series B preferred stock, at a purchase price per share of \$2.00, for an aggregate purchase price of \$48,200,000, and immediately following the first sale of shares of our series B preferred stock in April 2013, each of Plio Limited and Delphi Ventures, which purchased 3,000,000 and 2,500,000 shares,

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respectively, of our series B preferred stock, became a beneficial owner of more than 5% of our voting securities.

The following table sets forth the number of shares of series B preferred stock that were issued to holders of more than 5% of our voting securities at the time of such issuance, and affiliates of such holders, in connection with the series B preferred stock financing and the aggregate cash purchase price paid by such entities.

Purchaser	Shares of Series B	
	Preferred Stock	Purchase Price
Chione Ltd.	6,000,000	\$ 12,000,000
Plio Limited	9,000,000	\$ 18,000,000
Delphi Ventures and affiliates(1)	5,000,000	\$ 10,000,000

- (1) Consists of 4,951,650 shares purchased by Delphi Ventures VIII, L.P. and 48,350 shares purchased by Delphi BioInvestments VIII, L.P.

Series A-4 Preferred Stock Financing

In February 2012, we entered into a stock purchase agreement for the purpose of issuing and selling up to an aggregate of 1,538,461 shares of our series A-4 preferred stock, at a purchase price per share of \$1.30, for an aggregate purchase price of \$1,999,999. We issued these shares in August 2013.

The following table sets forth the number of shares of series A-4 preferred stock that were issued to a holder of more than 5% of our voting securities at the time of such issuance in connection with the series A-4 preferred stock financing and the aggregate cash purchase price paid by such entity.

Purchaser	Shares of Series A-4	
	Preferred Stock	Purchase Price
Plio Limited	1,538,461	\$ 1,999,999

Series A-2 and A-3 Preferred Stock Financing

In October 2011, we entered into a stock purchase agreement for the purpose of issuing and selling up to an aggregate of (i) 7,000,000 shares of our series A-2 preferred stock and (ii) 3,000,000 shares of our series A-3 preferred stock. Between October 2011 and February 2013, we became obligated to issue 6,100,000 shares of our series A-2 preferred stock at a purchase price per share of \$1.15, for an aggregate purchase price of \$7,015,000, and 1,764,706 shares of our series A-3 preferred stock at a purchase price per share of \$1.70, for an aggregate purchase price of \$3,000,000. We issued these shares in August 2013.

The following table sets forth the number of shares of series A-2 preferred stock and series A-3 preferred stock that were issued to a holder of more than 5% of our voting securities at the time of such issuance in connection with the series A-2 and series A-3 preferred stock financing and the aggregate cash purchase price paid by such entity.

Purchaser	Shares of Series A-2	Shares of Series A-3	Aggregate Purchase Price
	Preferred Stock	Preferred Stock	
Chione Ltd.	6,086,957	1,764,706	\$ 10,000,001

Series A Preferred Stock Financing

Between October 2010 and January 2013, we issued and sold an aggregate of 20,937,500 shares of our series A preferred stock, at a purchase price per share of \$1.00, for an aggregate purchase price of \$20,937,500. Immediately following the first sale of shares of our series A preferred stock in October

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2010, Chione Ltd., which purchased 5,000,000 shares of our series A preferred stock in such sale, became a beneficial owner of more than 5% of our voting securities.

The following table sets forth the number of shares of series A preferred stock that were issued to our directors, executive officers and holders of more than 5% of our voting securities at the time of such issuance in connection with the series A preferred stock financing and the aggregate cash purchase price paid by such persons and entities.

Purchaser	Shares of Series A Preferred Stock	Purchase Price
Michael G. Kauffman, M.D., Ph.D.	437,500	\$ 437,500
Chione Ltd.	15,000,000(1)	\$ 15,000,000

(1)

Does not include 5,000,000 shares of our series A preferred stock issued to Chione Ltd. in October 2010 at the initial closing of the series A preferred stock financing. Chione Ltd. became a beneficial owner of more than 5% of our voting securities immediately following such initial closing and we issued the 15,000,000 shares of our series A preferred stock listed in this table to Chione Ltd. after Chione Ltd. had become a holder of more than 5% of our voting securities.

Registration Rights

We are a party to a third amended and restated investors' rights agreement with the former holders of our preferred stock, including certain of our directors, executive officers and 5% stockholders and their affiliates. The investor rights agreement provides these holders the right to demand that we file a registration statement or request that their shares be covered by a registration statement that we are otherwise filing. See "Description of Capital Stock Registration Rights" for additional information regarding these registration rights.

Severance and Change in Control Agreements

See the "Executive Compensation Employment Agreements, Severance and Change in Control Arrangements" section of this prospectus for a further discussion of these arrangements.

Indemnification of Directors

Our certificate of incorporation limits the personal liability of directors for breach of fiduciary duty to the maximum extent permitted by the Delaware General Corporation Law and provides that no director will have personal liability to us or to our stockholders for monetary damages for any breach of fiduciary duty as a director. In addition, we have entered into indemnification agreements with each of our directors that require us, among other things, to indemnify each director for certain expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by him or her in any action or proceeding arising out of his or her service as one of our directors. See the "Executive Compensation Limitation of Liability and Indemnification" section of this prospectus for a further discussion of these arrangements.

Consulting Arrangements

We are party to a consulting agreement with Mirza Consulting, an entity that is wholly owned by Mansoor Raza Mirza, a member of our board of directors. Pursuant to this agreement, we pay Dr. Mirza (through such entity) a consulting fee of \$28,500 per month. Prior to January 1, 2013, we paid Dr. Mirza (through such entity) a consulting fee of \$10,000 per month. In December 2012, we issued an option to purchase 12,121 shares of our common stock to Mirza Consulting at an exercise price of \$1.49 per share.

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We are also a party to a consulting agreement with Dr. Tami Rashal, the sister of Dr. Sharon Shacham, our President and Chief Scientific Officer, and the sister-in-law of Michael Kauffman, our Chief Executive Officer and member of our board of directors. Pursuant to this agreement, we pay Dr. Rashal a consulting fee of \$12,083.33 per month, effective January 1, 2014. We also paid Dr. Rashal a bonus of \$19,500 for her services in 2013. Prior to January 1, 2014, we paid Dr. Rashal a consulting fee of \$11,666.66 per month, effective May 1, 2013. Prior to May 1, 2013, we paid Dr. Rashal a consulting fee of \$60 per hour, which fee was limited to \$10,000 per year. In September 2013, we granted to Dr. Rashal an option to purchase 15,151 shares of our common stock at an exercise price of \$4.75 per share.

Policies and Procedures for Related Person Transactions

On October 8, 2013, our board adopted written policies and procedures for the review of any transaction, arrangement or relationship in which we are a participant, the amount involved exceeds \$120,000, and one of our executive officers, directors, director nominees or 5% stockholders (or their immediate family members), each of whom we refer to as a "related person," has a direct or indirect material interest.

If a related person proposes to enter into such a transaction, arrangement or relationship, which we refer to as a "related person transaction," the related person must report the proposed related person transaction to our principal financial officer. The policy calls for the proposed related person transaction to be reviewed and, if deemed appropriate, approved by the board's audit committee. Whenever practicable, the reporting, review and approval will occur prior to effectiveness or consummation of the related person transaction. If advance review and approval is not practicable, the committee will review, and, in its discretion, may ratify the related person transaction. The policy also permits the chairman of the committee to review and, if deemed appropriate, approve proposed related person transactions that arise between committee meetings, subject to ratification by the committee at its next meeting. Any related person transactions that are ongoing in nature will be reviewed annually.

A related person transaction reviewed under the policy will be considered approved or ratified if it is authorized by the committee after full disclosure of the related person's interest in the transaction. As appropriate for the circumstances, the committee will review and consider:

the related person's interest in the related person transaction;

the approximate dollar value of the amount involved in the related person transaction;

the approximate dollar value of the amount of the related person's interest in the transaction without regard to the amount of any profit or loss;

whether the transaction was undertaken in the ordinary course of our business;

whether the terms of the transaction are no less favorable to us than terms that could have been reached with an unrelated third party;

the purpose of, and the potential benefits to us of, the transaction; and

any other information regarding the related person transaction or the related person in the context of the proposed transaction that would be material to investors in light of the circumstances of the particular transaction.

The committee may approve or ratify the related person transaction only if the committee determines that, under all of the circumstances, the transaction is in, or is not inconsistent with, our best interests. The committee may impose any conditions on the related person transaction that it deems appropriate.

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In addition to the transactions that are excluded by the instructions to the SEC's related person transaction disclosure rule, the board has determined that the following transactions do not create a material direct or indirect interest on behalf of related persons and, therefore, are not related person transactions for purposes of this policy:

interests arising solely from the related person's position as an executive officer of another entity (whether or not the person is also a director of such entity), that is a participant in the transaction, where (a) the related person and all other related persons own in the aggregate less than a 10% equity interest in such entity, (b) the related person and his or her immediate family members are not involved in the negotiation of the terms of the transaction and do not receive any special benefits as a result of the transaction, and (c) the amount involved in the transaction equals less than the greater of \$200,000 or 5% of the annual consolidated gross revenues of the company receiving payment under the transaction; and

a transaction that is specifically contemplated by provisions of our charter or bylaws.

The policy provides that transactions involving compensation of executive officers shall be reviewed and approved by the compensation committee in the manner specified in its charter.

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PRINCIPAL AND SELLING STOCKHOLDERS

The following table sets forth information with respect to the beneficial ownership of our common stock, as of February 28, 2014, by:

each person, or group of affiliated persons, known by us to beneficially own more than 5% of our common stock;

each of our directors;

each of our named executive officers;

all of our executive officers and directors as a group; and

each of the selling stockholders.

The column entitled "Shares Beneficially Owned Prior to Offering Percentage" is based on a total of 29,753,726 shares of our common stock outstanding as of February 28, 2014. The column entitled "Shares Beneficially Owned After Offering Percentage" is based on shares of our common stock to be outstanding after this offering, including _____ shares of our common stock that we are selling in this offering, and _____ shares of our common stock that the selling stockholders are selling in this offering, each at an assumed public offering price of \$ _____ per share, which was the last reported sale price of our common stock on The Nasdaq Global Select Market on _____, 2014, but not including any additional shares issuable upon exercise of outstanding options or the underwriters' over-allotment option.

The number of shares beneficially owned by each stockholder is determined under rules issued by the Securities and Exchange Commission and includes voting or investment power with respect to securities. Under these rules, beneficial ownership includes any shares as to which the individual or entity has sole or shared voting power or investment power. In computing the number of shares beneficially owned by an individual or entity and the percentage ownership of that person, shares of common stock subject to options or other rights held by such person that are currently exercisable or will become exercisable within 60 days of February 28, 2014, are considered outstanding, although such shares subject to options or other rights are not considered outstanding for purposes of computing the percentage ownership of any other person. Unless otherwise indicated, the address of all listed stockholders is c/o Karyopharm Therapeutics Inc., 2 Mercer Road, Natick, Massachusetts 01760. Each of the stockholders listed has sole voting and investment power with respect to the shares beneficially owned by the stockholder unless noted otherwise, subject to community property laws where applicable.

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The table below does not reflect any shares of our common stock that our directors, executive officers, 5% stockholders or their affiliated entities may purchase in this offering.

Name of Beneficial Owner	Shares Beneficially Owned Prior to Offering		Shares Beneficially Owned After Offering	
	Number	Percentage	Number	Percentage
5% Stockholders				
Chione Ltd.(1)	10,258,079	34.48%		
Plio Limited(2)	3,193,473	10.73%		
Entities Affiliated with Foresite Capital(3)	2,378,615	7.99%		
Entities Affiliated with FMR LLC(4)	2,346,000	7.88%		
Entities Affiliated with Delphi Ventures(5)	2,103,133	7.07%		
Named Executive Officers and Directors				
Michael G. Kauffman, M.D., Ph.D.(6)	1,960,306	6.59%		
Sharon Shacham, Ph.D., M.B.A.(7)	1,960,306	6.59%		
Paul Brannelly	63,636	*		
Deepa R. Pakianathan, Ph.D.(8)	2,103,133	7.07%		
Mansoor Raza Mirza, M.D.(9)	48,100	*		
Alan T. Barber(10)	10,290	*		
Barry E. Greene(11)	4,640	*		
Kenneth E. Weg(12)	2,209	*		
Garen Bohlin	0	*		
All executive officers and directors as a group (9 persons)(13)	4,192,314	14.09%		
Certain other selling stockholders(14)				
All selling stockholders(14)				

*

Less than 1%.

(1)

The address for Chione Ltd. is Simou Menardou 8, Ria Court 8, Office 101, 6015 Larnaca, Cyprus. The board of directors of Chione, comprised of Marcin Czernik, Andreas Hadjimichael and Amalia Hadjimichael, and its sole stockholder, Wiaczeslaw Smolokowski, may be deemed to share voting and investment power with respect to the shares held by such entity and each of them disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein. The shares held by Chione Ltd. do not include the shares held by Plio Limited.

(2)

The address for Plio Limited is Simou Menardou 8, Ria Court 8, Office 101, 6015 Larnaca, Cyprus. The board of directors of Plio, comprised of Marcin Czernik, Andreas Hadjimichael and Amalia Hadjimichael, and its sole stockholder, Gregory Jankilevitch, may be deemed to share voting and investment power with respect to the shares held by such entity and each of them disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein. The shares held by Plio Limited do not include the shares held by Chione Ltd.

(3)

The address for Foresite Capital and affiliates is One Montgomery Street, Suite 2500, San Francisco, California 94104. Consists of (i) 1,585,743 shares of common stock held by Foresite Capital Fund I, L.P. (ii) 688,705 shares of common stock held by Foresite Capital IV-B, LLC and (iii) 104,167 shares of common stock held by Foresite Capital IV-C, LLC. James B. Tananbaum is the managing member of Foresite Capital Management I, LLC, the general partner of Foresite Capital Fund I, L.P., is the managing member of Foresite Capital IV-B Management, LLC, the managing member of Foresite Capital IV-B, LLC, and is the managing member of Foresite Capital IV-C Management, LLC, the managing member of Foresite Capital IV-C, LLC, and as such, James B. Tananbaum may be deemed to have sole voting and investment power over the securities held by Foresite Capital Fund I, L.P., Foresite Capital

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IV-B, LLC and Foresite Capital IV-C, LLC. James B. Tananbaum disclaims beneficial ownership of these securities except to the extent of his pecuniary interest therein. For information regarding Foresite Capital and its affiliates, we have relied on the Schedule 13G filed by Foresite Capital Fund I, L.P. filed with the SEC on November 15, 2013.

- (4) The address for Fidelity SelectCo, LLC ("SelectCo") is 1225 17th Street, Suite 1100, Denver, Colorado 80202 and the address for Fidelity Select Biotechnology Portfolio ("Portfolio") is 245 Summer Street, Boston, Massachusetts 02210. SelectCo, a wholly-owned subsidiary of FMR LLC and an investment adviser registered under Section 203 of the Investment Advisers Act of 1940, may be deemed to be the beneficial owner of 2,346,000 shares of common stock as a result of acting as investment adviser to various investment companies registered under Section 8 of the Investment Company Act of 1940, including Portfolio, which holds 2,055,682 shares of common stock. Additional shares of common stock are owned by other investment companies. Members of the family of Edward C. Johnson 3d, Chairman of FMR LLC, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. For information regarding FMR LLC and its affiliates, we have relied on the Schedule 13G filed by FMR LLC with the SEC on February 14, 2014.
- (5) The address for Delphi Ventures and affiliates is 3000 Sand Hill Road, #1-135, Menlo Park, California 94025. Delphi Ventures VIII, L.P. ("Delphi VIII") directly holds 2,082,796 shares prior to this offering. Delphi BioInvestments VIII, L.P. ("DBI VIII") directly holds 20,337 shares prior to this offering. Delphi Management Partners VIII, L.L.C. ("DMP VIII") is the general partner of Delphi VIII and DBI VIII (together, the "Delphi VIII Funds") and may be deemed to have sole voting and dispositive power over the shares held by the Delphi VIII Funds. DMP VIII and each of James J. Bochnowski, David L. Douglass, Douglas A. Roeder and Deepa R. Pakianathan, Ph.D., the Managing Members of DMP VIII who may be deemed to share voting and dispositive power over the reported securities, disclaim beneficial ownership of the reported securities held by Delphi VIII Funds except to the extent of any pecuniary interest therein.
- (6) Consists of (a) 40,024 shares of common stock underlying options held by Michael Kauffman that are exercisable as of February 28, 2014 or will become exercisable within 60 days after such date, (b) 830,171 shares of common stock held by Michael Kauffman, (c) 171,148 shares of common stock underlying options held by Sharon Shacham, who is the spouse of Michael Kauffman, that are exercisable as of February 28, 2014 or will become exercisable within 60 days after such date and (d) 918,963 shares of common stock held by Sharon Shacham.
- (7) Consists of (a) 171,148 shares of common stock underlying options held by Sharon Shacham that are exercisable as of February 28, 2014 or will become exercisable within 60 days after such date, (b) 918,963 shares of common stock held by Sharon Shacham, (c) 40,024 shares of common stock underlying options held by Michael Kauffman, who is Sharon Shacham's spouse, that are exercisable as of February 28, 2014 or will become exercisable within 60 days after such date and (d) 830,171 shares of common stock held by Michael Kauffman.
- (8) Delphi Ventures VIII, L.P. ("Delphi VIII") directly holds 2,082,796 shares prior to this offering. Delphi BioInvestments VIII, L.P. ("DBI VIII") directly holds 20,337 shares prior to this offering. Delphi Management Partners VIII, L.L.C. ("DMP VIII") is the general partner of Delphi VIII and DBI VIII (together, the "Delphi VIII Funds") and may be deemed to have sole voting and dispositive power over the shares held by the Delphi VIII Funds. DMP VIII and each of James J. Bochnowski, David L. Douglass, Douglas A. Roeder and Deepa R. Pakianathan, Ph.D., the Managing Members of DMP VIII who may be deemed to share voting and dispositive power over the reported securities, disclaim beneficial ownership of the reported securities held by Delphi VIII Funds except to the extent of any pecuniary interest therein.

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- (9) Consists of (a) 25,373 shares of common stock underlying options that are exercisable as of February 28, 2014 or will become exercisable within 60 days after such date and (b) 22,727 shares of common stock.
- (10) Consists of 10,290 shares of common stock underlying options that are exercisable as of February 28, 2014 or will become exercisable within 60 days after such date.
- (11) Consists of 4,640 shares of common stock underlying options that are exercisable as of February 28, 2014 or will become exercisable within 60 days after such date.
- (12) Consists of 2,209 shares of common stock that are exercisable as of February 28, 2014 or will become exercisable within 60 days after such date.
- (13) Includes 253,684 shares of common stock underlying options that are exercisable as of February 28, 2014 or will become exercisable within 60 days after such date.
- (14) Selling stockholder information to be provided by filing of an amendment to the registration statement of which this prospectus forms a part.

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DESCRIPTION OF CAPITAL STOCK

General

Our authorized capital stock consists of 100,000,000 shares of common stock, par value \$0.0001 per share, and 5,000,000 shares of preferred stock, par value \$0.0001 per share. The following description of our capital stock and provisions of our certificate of incorporation and by-laws are summaries and are qualified by reference to our certificate of incorporation and by-laws. Copies of these documents have been filed with the Securities and Exchange Commission as exhibits to our registration statement, of which this prospectus forms a part.

Common Stock

As of December 31, 2013, there were 29,753,726 shares of our common stock outstanding and held of record by approximately 43 stockholders.

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. An election of directors by our stockholders shall be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend rights of any series of preferred stock that we may designate and issue in the future.

In the event of our liquidation or dissolution, the holders of common stock are entitled to receive proportionately our net assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the prior rights of any outstanding preferred stock. Holders of common stock have no preemptive, subscription, redemption or conversion rights. Our outstanding shares of common stock are, and the shares offered by us in this offering will be, when issued and paid for, validly issued, fully paid and nonassessable. The rights, preferences and privileges of holders of common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Preferred Stock

Under the terms of our certificate of incorporation, our board of directors is authorized to direct us to issue shares of preferred stock in one or more series without stockholder approval. Our board of directors has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock.

The purpose of authorizing our board of directors to issue preferred stock and determine its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions, future financings and other corporate purposes, could have the effect of making it more difficult for a third party to acquire, or could discourage a third party from seeking to acquire, a majority of our outstanding voting stock. As of December 31, 2013, there were no shares of preferred stock outstanding, and we have no present plans to issue any shares of preferred stock.

Options

As of December 31, 2013, options to purchase 2,410,522 shares of our common stock at a weighted average exercise price of \$7.85 per share were outstanding.

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Registration Rights

We have entered into a third amended and restated investors' rights agreement, dated July 26, 2013, which we refer to as the investor rights agreement, with the former holders of shares of our preferred stock. Holders of a total of 18,981,667 shares of our common stock as of December 31, 2013 have the right to require us to register these shares under the Securities Act, and to participate in future registrations of securities by us, under the circumstances described below. After registration pursuant to these rights, these shares will become freely tradable without restriction under the Securities Act except that affiliates will need to comply with resale restrictions under Rule 144 of the Securities Act. If not otherwise exercised, the rights described below will expire five years after the closing of our initial public offering.

Demand Registration Rights

Beginning 180 days after the effective date of the registration statement relating to our initial public offering, subject to specified limitations set forth in the investor rights agreement, at any time, the holders of 50% or more of the then outstanding shares having rights under the investor rights agreement, which we refer to as registrable shares, may at any time demand in writing that we register all or a portion of the registrable shares under the Securities Act if the total amount of registrable shares registered have an anticipated aggregate offering price of at least \$5,000,000. We are not obligated to file a registration statement pursuant to this provision on more than two occasions.

In addition, subject to specified limitations set forth in the investor rights agreement, at any time after we become eligible to file a registration statement on Form S-3, holders of registrable shares outstanding may demand that we register on Form S-3 the registrable shares held by them so long as the total amount of registrable shares being registered has an aggregate offering price of at least \$1,000,000. We are not obligated to file a registration statement pursuant to this provision on more than two occasions in any 12-month period.

Incidental Registration Rights

If we propose to file a registration statement to register any of our securities under the Securities Act, either for our own account or for the account of any of our stockholders, other than pursuant to the demand registration rights described above and other than pursuant to a Form S-4 or Form S-8, the holders of our registrable shares are entitled to notice of registration and, subject to specified limitations set forth in the investor rights agreement, we will be required to use best efforts to register the registrable shares then held by them that they request that we register.

In the event that any registration in which the holders of registrable shares participate pursuant to our investor rights agreement is an underwritten public offering, we agree to enter into an underwriting agreement containing customary representations and warranties and covenants.

In the event that any registration in which the holders of registrable shares participate pursuant to our investor rights agreement is an underwritten public offering, we will use our best efforts to include the requested registrable shares to be included, but may be limited by market conditions.

Expenses

Pursuant to the investor rights agreement, we are required to pay all registration, qualification and filing fees, printing and accounting expenses, fees and expenses of one counsel to represent the selling stockholders and other reasonable direct costs for the selling stockholders (such selling stockholder expenses not to exceed \$50,000), but excluding underwriting discounts, selling commissions and the fees and expenses of selling stockholders' own counsel (other than the counsel selected to represent all selling stockholders). We are not required to pay registration expenses if the registration

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request under the investor rights agreement is withdrawn at the request of holders of a majority of the registrable shares, unless such holders agree to forfeit their right to one demand registration, or the withdrawal is due to discovery of a materially adverse change in our business.

The investor rights agreement contains customary cross-indemnification provisions, pursuant to which we are obligated to indemnify the selling stockholders in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions in the registration statement attributable to them.

Anti-Takeover Provisions

We are subject to Section 203 of the Delaware General Corporation Law. Subject to certain exceptions, Section 203 prevents a publicly held Delaware corporation from engaging in a "business combination" with any "interested stockholder" for three years following the date that the person became an interested stockholder, unless the interested stockholder attained such status with the approval of our board of directors or unless the business combination is approved in a prescribed manner or the interested stockholder acquired at least 85% of our outstanding voting stock in the transaction in which it became an interested stockholder. A "business combination" includes, among other things, a merger or consolidation involving us and the "interested stockholder" and the sale of more than 10% of our assets. In general, an "interested stockholder" is any entity or person beneficially owning 15% or more of our outstanding voting stock and any entity or person affiliated with or controlling or controlled by such entity or person.

Staggered Board; Removal of Directors

Our certificate of incorporation and our by-laws divide our board of directors into three classes with staggered three-year terms. In addition, such certificate of incorporation and by-laws provide that, subject to the rights of holders of any series of preferred stock, a director may be removed only for cause and only by the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in an annual election of directors. Under our certificate of incorporation and by-laws, any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office. Furthermore, our certificate of incorporation provides that the authorized number of directors may be changed only by the resolutions of our board of directors.

The classification of our board of directors and the limitations on the removal of directors and filling of vacancies could make it more difficult for a third party to acquire, or discourage a third party from seeking to acquire, control of our company.

Super-Majority Voting

The Delaware General Corporation Law provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or by-laws, unless a corporation's certificate of incorporation or by-laws, as the case may be, requires a greater percentage. Our by-laws may be amended or repealed by a majority vote of our board of directors or the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in any annual election of directors. In addition, the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in any annual election of directors is required to amend or repeal, or to adopt any provisions inconsistent with, any of the provisions of our certificate of incorporation described under "Staggered Board; Removal of Directors" above.

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Stockholder Action; Special Meeting of Stockholders; Advance Notice Requirements for Stockholder Proposals and Director Nominations

Our certificate of incorporation and our by-laws provide that any action required or permitted to be taken by our stockholders at a duly called annual meeting or special meeting of stockholders may only be taken if it is properly brought before such meeting and may not be taken by written action in lieu of a meeting. Our certificate of incorporation and our by-laws also provide that, except as otherwise required by law, special meetings of our stockholders can only be called by our board of directors, chairman of the board or chief executive officer. In addition, our by-laws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of stockholders, including proposed nominations of candidates for election to our board of directors. Stockholders at an annual meeting may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of our board of directors, or by a stockholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has delivered timely written notice in proper form to our secretary of the stockholder's intention to bring such business before the meeting. These provisions could have the effect of delaying until the next stockholder meeting stockholder actions that are favored by the holders of a majority of our outstanding voting stock. These provisions also could discourage a third party from making a tender offer for our common stock, because even if it acquired a majority of our outstanding voting stock, it would be able to take action as a stockholder, such as electing new directors or approving a merger, only at a duly called stockholders meeting and not by written consent.

Authorized But Unissued Shares

The authorized but unissued shares of common stock and preferred stock are available for future issuance without stockholder approval, subject to any limitations imposed by the listing standards of The NASDAQ Global Select Market. These additional shares may be used for a variety of corporate finance transactions, acquisitions and employee benefit plans. The existence of authorized but unissued and unreserved common stock and preferred stock could make more difficult or discourage an attempt to obtain control of us by means of a proxy contest, tender offer, merger or otherwise.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A.

NASDAQ Global Select Market

Our common stock is listed on The NASDAQ Global Select Market under the symbol "KPTI."

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SHARES ELIGIBLE FOR FUTURE SALE

Future sales of substantial amounts of common stock in the public market, or the perception that such sales may occur, could adversely affect the market price of our common stock. Our common stock is listed on The NASDAQ Global Select Market under the symbol "KPTI."

Upon the closing of this offering, we will have outstanding an aggregate of _____ shares of common stock, based on the number of shares of our common stock outstanding as of December 31, 2013, assuming the issuance of _____ shares of common stock by us in this offering and assuming no exercise by the underwriters of their over-allotment option and no exercise of options outstanding as of December 31, 2013. Of these shares, all shares sold in this offering, including both the shares sold by us and the shares sold by the selling stockholders, will be freely tradable without restriction or further registration under the Securities Act, except for any shares purchased by our "affiliates," as that term is defined in Rule 144 under the Securities Act, whose sales would be subject to the Rule 144 resale restrictions described below, other than the holding period requirement.

The remaining _____ shares of common stock will be "restricted securities," as that term is defined in Rule 144 under the Securities Act, of which _____ shares of common stock will further be subject to either restrictions on transfer under the lock-up agreements described below, under the lock-up agreements entered into in connection with our initial public offering or restrictions on transfer under stock option agreements or the investor rights agreement entered into between us and the holders of those shares. The lock-up agreements entered into in connection with this offering restrict transfer for a period of 90 days from the effectiveness of the registration statement of which this prospectus forms a part. The lock-up agreements entered into in connection with our initial public offering and the restrictions on transfer under stock option agreements and the investor rights agreement provide for a 180-day lock period in connection with our initial public offering, which period expires on May 4, 2014. Following the expiration of these restrictions, these shares will become eligible for public sale if they are registered under the Securities Act or if they qualify for an exemption from registration under Rules 144 or 701 under the Securities Act, which are summarized below.

In addition, of the 2,410,522 shares of our common stock that were subject to stock options outstanding as of December 31, 2013, options to purchase 317,804 shares of common stock were vested as of December 31, 2013 and, upon exercise, these shares will be eligible for sale, subject to the lock-up agreements described in this section and Rules 144 and 701 under the Securities Act.

Lock-Up Agreements

We and each of our directors and executive officers and the selling stockholders, who collectively own _____ shares of our common stock as of December 31, 2013, without the prior written consent of Merrill Lynch, Pierce, Fenner & Smith Incorporated on behalf of the underwriters, will not, subject to limited exceptions, during the period ending 90 days from the effectiveness of the registration statement of which this prospectus forms a part, directly or indirectly:

offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant for the sale of, or otherwise dispose of or transfer any shares of our common stock or any securities convertible into or exchangeable or exercisable for our common stock, except for the shares made available by our selling stockholders as part of this prospectus;

exercise any right with respect to the registration of any shares of our common stock or any security convertible into or exercisable or exchangeable for our common stock, or with respect to the filing of any registration statement in connection therewith under the Securities Act; or

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enter into any swap or any other agreement or any transaction that transfers, in whole or in part, the economic consequence of ownership of our common stock,

whether any transaction described above is to be settled by delivery of our common stock or such other securities, in cash or otherwise.

The lock-up restrictions are described in more detail in the section of this prospectus entitled "Underwriting."

Rule 144

Affiliate Resales of Restricted Securities

In general, a person who is an affiliate of ours, or who was an affiliate at any time during the 90 days before a sale, who has beneficially owned shares of our common stock for at least six months would be entitled to sell in "broker's transactions" or certain "riskless principal transactions" or to market makers, a number of shares within any three-month period that does not exceed the greater of:

1% of the number of shares of our common stock then outstanding, which will equal approximately _____ shares immediately after this offering; or

the average weekly trading volume in our common stock on The NASDAQ Global Select Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to such sale.

Affiliate resales under Rule 144 are also subject to the availability of current public information about us. In addition, if the number of shares being sold under Rule 144 by an affiliate during any three-month period exceeds 5,000 shares or has an aggregate sale price in excess of \$50,000, the seller must file a notice on Form 144 with the Securities and Exchange Commission and NASDAQ concurrently with either the placing of a sale order with the broker or the execution directly with a market maker.

Non-Affiliate Resales of Restricted Securities

In general, a person who is not an affiliate of ours at the time of sale, and has not been an affiliate at any time during the 90 days preceding a sale, and who has beneficially owned shares of our common stock for at least six months but less than a year, is entitled to sell such shares subject only to the availability of current public information about us. If such person has held our shares for at least one year, such person can resell under Rule 144(b)(1) without regard to any Rule 144 restrictions, including the current public information requirement.

Non-affiliate resales are not subject to the manner of sale, volume limitation or notice filing provisions of Rule 144.

Rule 701

In general, under Rule 701, any of an issuer's employees, directors, officers, consultants or advisors who purchases shares from the issuer in connection with a qualified compensatory stock or option plan or other written agreement before our initial public offering is entitled to sell such shares in reliance on Rule 144. An affiliate of the issuer can resell shares in reliance on Rule 144 without having to comply with the holding period requirement, and non-affiliates of the issuer can resell shares in reliance on Rule 144 without having to comply with the current public information and holding period requirements.

The Securities and Exchange Commission has indicated that Rule 701 will apply to typical stock options granted by an issuer before it becomes subject to the reporting requirements of the

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Securities Exchange Act of 1934, as amended, or the Exchange Act, along with the shares acquired upon exercise of such options, including exercises after an issuer becomes subject to the reporting requirements of the Exchange Act.

Equity Plans

We have filed a registration statement on Form S-8 under the Securities Act to register all shares of common stock subject to outstanding stock options and common stock issuable under our stock plans, permitting the resale of such shares by non-affiliates in the public market without restriction under the Securities Act and the sale by affiliates in the public market, subject to compliance with the resale provisions of Rule 144.

Registration Rights

As of December, 31, 2013, the holders of 18,981,667 shares of our common stock or their transferees are entitled to various rights with respect to the registration of these shares under the Securities Act. Registration of these shares under the Securities Act would result in these shares becoming fully tradable without restriction under the Securities Act immediately upon the effectiveness of the registration, subject to the terms of the lock-up agreement to which the holder is subject and except for shares purchased by affiliates. See "Description of Capital Stock Registration Rights" for additional information.

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**MATERIAL U.S. FEDERAL TAX CONSIDERATIONS FOR NON-U.S. HOLDERS
OF COMMON STOCK**

The following is a general discussion of material U.S. federal income and estate tax considerations relating to the purchase, ownership and disposition of shares of our common stock by a non-U.S. holder. For purposes of this discussion, the term "non-U.S. holder" means a beneficial owner of shares of our common stock that is, for U.S. federal income tax purposes, an individual, corporation (or other entity treated as a corporation), estate or trust other than:

an individual who is a citizen or resident of the United States;

a corporation, or other entity treated as a corporation for U.S. federal income tax purposes, created or organized in or under the laws of the United States or of any state or political subdivision of the United States;

an estate the income of which is subject to U.S. federal income taxation regardless of its source; or

a trust, if a U.S. court is able to exercise primary supervision over the administration of the trust and one or more U.S. persons have authority to control all substantial decisions of the trust or if the trust has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person.

This discussion is based on current provisions of the U.S. Internal Revenue Code of 1986, as amended, which we refer to as the Code, existing and proposed U.S. Treasury Regulations promulgated or proposed thereunder and current administrative and judicial interpretations thereof, all as in effect as of the date of this prospectus and all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any change could alter the tax consequences to non-U.S. holders described in this prospectus. In addition, the Internal Revenue Service, or the IRS, could challenge one or more of the tax consequences described in this prospectus.

We assume in this discussion that each non-U.S. holder holds shares of our common stock as a capital asset (generally, property held for investment). This discussion does not address all aspects of U.S. federal income and estate taxation, including the Medicare contribution tax, that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder's individual circumstances nor does it address any aspects of U.S. state, local or non- U.S. taxes, or, except as explicitly addressed herein, U.S. federal taxes other than income and estate taxes. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax considerations that may be applicable to particular non-U.S. holders, such as:

insurance companies;

tax-exempt organizations;

financial institutions;

brokers or dealers in securities;

regulated investment companies;

pension plans;

controlled foreign corporations;

passive foreign investment companies;

corporations that accumulate earnings to avoid U.S. federal income tax;

persons subject to the alternative minimum tax;

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persons that have a "functional currency" other than the U.S. dollar;

persons that acquire shares of our common stock as compensation for services;

owners that hold shares of our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment; and

certain U.S. expatriates.

In addition, this discussion does not address the tax treatment of partnerships or persons who hold their shares of our common stock through partnerships or other entities which are pass-through entities for U.S. federal income tax purposes. A partner in a partnership or other pass-through entity that will hold shares of our common stock should consult his, her or its own tax advisor regarding the tax consequences of the ownership and disposition of our common stock through a partnership or other pass-through entity, as applicable.

Prospective investors should consult their own tax advisors regarding the U.S. federal, state, local and non- U.S. income and other tax considerations of acquiring, holding and disposing of shares of our common stock.

Dividends

If we pay distributions of cash or property with respect to shares of our common stock, those distributions generally will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles and will be subject to withholding as described in the paragraphs below. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder's investment, up to such holder's tax basis in its shares of our common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below under the heading "Gain on Sale, Exchange or Other Taxable Disposition of Shares of Our Common Stock." Any such distributions will also be subject to the discussion below under the section titled "Withholding and Information Reporting Requirements FATCA."

Subject to the exceptions described below, dividends paid to a non-U.S. holder generally will be subject to withholding of U.S. federal income tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence. If we determine, at a time reasonably close to the date of payment of a distribution on shares of our common stock, that the distribution will not constitute a dividend because we do not anticipate having current or accumulated earnings and profits, we intend not to withhold any U.S. federal income tax on the distribution as permitted by U.S. Treasury Regulations; otherwise, we intend to withhold the appropriate amount of U.S. federal income tax on the distribution.

Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States, and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States, are generally exempt from the 30% withholding tax if the non- U.S. holder satisfies applicable certification and disclosure requirements. To obtain this exemption, a non-U.S. holder must generally provide us with a properly executed IRS Form W-8ECI properly certifying such exemption. However, such U.S. effectively connected income, net of specified deductions and credits, is taxed at the same graduated U.S. federal income tax rates applicable to U.S. persons (as defined in the Code). Any U.S. effectively connected income received by a non-U.S. holder that is treated as a corporation for U.S. federal income tax purposes may also, under certain circumstances, be subject to an additional "branch profits tax" at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence.

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A non-U.S. holder of shares of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder's country of residence generally will be required to provide a properly executed IRS Form W-8BEN (or successor form) and satisfy applicable certification and other requirements. Non-U.S. holders are urged to consult their own tax advisors regarding their entitlement to benefits under a relevant income tax treaty.

A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty or that is otherwise not subject to U.S. withholding tax may obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim with the IRS.

Gain on Sale, Exchange or Other Taxable Disposition of Shares of Our Common Stock

Subject to the discussion below under the section titled "Withholding and Information Reporting Requirements FATCA," a non-U.S. holder generally will not be subject to U.S. federal income tax on gain realized on a sale, exchange or other taxable disposition of shares of our common stock unless:

the gain is effectively connected with the non-U.S. holder's conduct of a trade or business in the United States, and, if an applicable income tax treaty so provides, the gain is attributable to a permanent establishment or fixed base maintained by the non-U.S. holder in the United States; in these cases, the non-U.S. holder generally will be taxed on a net income basis at the regular graduated rates and in the manner applicable to U.S. persons, and, if the non-U.S. holder is a non-U.S. corporation, an additional branch profits tax at a rate of 30%, or a lower rate as may be specified by an applicable income tax treaty, may also apply;

the non-U.S. holder is a nonresident alien individual present in the United States for 183 days or more in the taxable year of the disposition and certain other conditions are met, in which case the non-U.S. holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty) on the net gain derived from the disposition, which may be offset by certain U.S. source capital losses of the non-U.S. holder, if any; or

we are or have been, at any time during the five-year period preceding such disposition (or the non-U.S. holder's holding period, if shorter) a "U.S. real property holding corporation" unless our common stock is regularly traded on an established securities market and the non-U.S. holder held no more than 5% of our outstanding common stock, directly or indirectly, during the shorter of the 5-year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. Generally, a corporation is a "U.S. real property holding corporation" if the fair market value of its "U.S. real property interests" (within the meaning of the Code) equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we believe that we are not currently, and we do not anticipate becoming, a "U.S. real property holding corporation" for U.S. federal income tax purposes. No assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of the rules described above.

Information Reporting and Backup Withholding Tax

We must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on shares of our common stock paid to such holder and the tax withheld, if any, with respect to such distributions. These information reporting requirements apply even if withholding is not required. Non-U.S. holders may have to comply with specific certification procedures to establish that the holder is not a U.S. person (as defined in the Code) or is otherwise subject to an exemption in order to avoid backup withholding at the applicable rate with respect to dividends paid with respect to

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shares of our common stock. Generally, a holder will comply with such procedures if it provides a properly executed IRS Form W-8BEN (or other applicable Form W-8) or otherwise meets documentary evidence requirements for establishing that it is a non-U.S. holder, or otherwise establishes an exemption. Dividends paid to non-U.S. holders subject to the U.S. federal withholding tax, as described above in "Dividends," generally will be exempt from U.S. backup withholding.

Information reporting and backup withholding generally will apply to the payment of the proceeds of a disposition of shares of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or non-U.S., unless the holder certifies that it is not a U.S. person (as defined in the Code) and satisfies certain other requirements, or otherwise establishes an exemption. For information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker and dispositions otherwise effected through a non-U.S. office generally will not be subject to information reporting. Generally, backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected through a non-U.S. office of a broker. Non-U.S. holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them.

Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder's U.S. federal income tax liability, if any, provided that an appropriate claim is timely filed with the IRS.

Withholding and Information Reporting Requirements FATCA

Legislation enacted in March 2010, which is commonly referred to as "FATCA," generally will impose a U.S. federal withholding tax at a rate of 30% on payments to certain non-U.S. entities (including intermediaries), of dividends on and the gross proceeds from the sale or other disposition of shares of our common stock unless such entities comply with a complicated U.S. information reporting, due diligence, disclosure and certification regime. This new regime and its requirements are different from, and in addition to, the certification requirements described elsewhere in this discussion. Withholding under FATCA will apply to (1) payments of dividends with respect to shares of our common stock made after June 30, 2014, and (2) payments of gross proceeds from a sale or other disposition of shares of our common stock made after December 31, 2016. Under certain circumstances, a non-U.S. holder may be eligible for refunds or credits of the tax. Non-U.S. holders should consult their own tax advisors regarding the possible impact of these rules on their investment in shares of our common stock, including any investment in shares of our common stock made through another entity or an intermediary.

U.S. Federal Estate Tax

Shares of our common stock owned or treated as owned at the time of death by an individual who is not a citizen or resident of the United States (as specially defined for U.S. federal estate tax purposes) will be included in the individual's gross estate for U.S. federal estate tax purposes and, therefore, may be subject to U.S. federal estate tax, unless an applicable estate tax or other treaty provides otherwise.

The preceding discussion of material U.S. federal tax considerations is for general information only. It is not tax advice. Prospective investors should consult their own tax advisors regarding the particular U.S. federal, state, local and non-U.S. tax consequences of purchasing, holding and disposing of shares of our common stock, including the consequences of any proposed changes in applicable laws.

Table of Contents**UNDERWRITING**

Merrill Lynch, Pierce, Fenner & Smith Incorporated and Leerink Partners LLC are acting as representatives of each of the underwriters named below. Subject to the terms and conditions set forth in an underwriting agreement among us, the selling stockholders and the underwriters, we and the selling stockholders have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us and the selling stockholders, the number of shares of common stock set forth opposite its name below.

<u>Underwriter</u>	<u>Number of Shares</u>
Merrill Lynch, Pierce, Fenner & Smith Incorporated	
Leerink Partners LLC	
JMP Securities LLC	
Wedbush Securities Inc	
Oppenheimer & Co. Inc.	
Total	

Subject to the terms and conditions set forth in the underwriting agreement, the underwriters have agreed, severally and not jointly, to purchase all of the shares sold under the underwriting agreement if any of these shares are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated.

We and the selling stockholders have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make in respect of those liabilities.

The underwriters are offering the shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel, including the validity of the shares, and other conditions contained in the underwriting agreement, such as the receipt by the underwriters of officers' certificates and legal opinions. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Commissions and Discounts

The representatives have advised us and the selling stockholders that the underwriters propose initially to offer the shares to the public at the public offering price set forth on the cover page of this prospectus and to dealers at that price less a concession not in excess of \$ per share. After the initial offering, the public offering price, concession or any other term of the offering may be changed.

The following table shows the public offering price, underwriting discount and proceeds before expenses to us and to the selling stockholders. We will not receive any of the proceeds from the sale of the common stock by the selling stockholders. The information assumes either no exercise or full exercise by the underwriters of their option to purchase additional shares of our common stock.

	Per Share	Without Option	With Option
Public offering price	\$	\$	\$
Underwriting discount	\$	\$	\$
Proceeds, before expenses, to us	\$	\$	\$
Proceeds, before expenses, to the selling stockholders	\$	\$	

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The expenses of the offering to us, not including the underwriting discount, are estimated at \$ _____ million. We have agreed to reimburse the underwriters for all expenses related to the clearing of this offering with the Financial Industry Regulatory Authority and the qualification of our common stock under state securities laws (in an amount not to exceed in the aggregate \$ _____).

Option to Purchase Additional Shares

We have granted an option to the underwriters, exercisable for 30 days after the date of this prospectus, to purchase up to _____ additional shares at the public offering price, less the underwriting discount. If the underwriters exercise this option, each will be obligated, subject to conditions contained in the underwriting agreement, to purchase a number of additional shares proportionate to that underwriter's initial amount reflected in the above table. The selling stockholders have not granted such an option to the underwriters.

No Sales of Similar Securities

We, our executive officers and directors and the selling stockholders have agreed not to sell or transfer any common stock or securities convertible into or exchangeable or exercisable for common stock, for 90 days after the date of this prospectus without first obtaining the written consent of Merrill Lynch, Pierce, Fenner & Smith Incorporated. Specifically, we and these other persons have agreed, with certain limited exceptions, not to directly or indirectly

offer, pledge, sell or contract to sell any common stock;

sell any option or contract to purchase any common stock;

purchase any option or contract to sell any common stock;

grant any option, right or warrant for the sale of any common stock;

otherwise dispose of or transfer any common stock;

request or demand that we file a registration statement related to the common stock; or

enter into any swap or other agreement or any transaction that transfers, in whole or in part, the economic consequence of ownership of any common stock, whether any such swap, agreement or transaction is to be settled by delivery of shares or other securities, in cash or otherwise.

This lock-up provision applies to common stock and to securities convertible into or exchangeable or exercisable for common stock. It also applies to common stock owned now or acquired later by the person executing the agreement or for which the person executing the agreement later acquires the power of disposition.

NASDAQ Global Select Market Listing

Our common stock is listed on the NASDAQ Global Select Market under the symbol "KPTI."

Price Stabilization, Short Positions

Until the distribution of the shares is completed, SEC rules may limit underwriters and selling group members from bidding for and purchasing our common stock. However, the representatives may engage in transactions that stabilize the price of the common stock, such as bids or purchases to peg, fix or maintain that price.

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In connection with the offering, the underwriters may purchase and sell our common stock in the open market. These transactions may include short sales, purchases on the open market to cover

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positions created by short sales and stabilizing transactions. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering. "Covered" short sales are sales made in an amount not greater than the underwriters' option described above. The underwriters may close out any covered short position by either exercising their option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option to purchase shares granted to them. "Naked" short sales are sales in excess of such option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of our common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of shares of common stock made by the underwriters in the open market prior to the completion of the offering.

Similar to other purchase transactions, the underwriters' purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. The underwriters may conduct these transactions on the NASDAQ Global Select Market, in the over-the-counter market or otherwise.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. In addition, neither we nor any of the underwriters make any representation that the representatives will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

Passive Market Making

In connection with this offering, underwriters and selling group members may engage in passive market making transactions in the common stock on the Nasdaq Global Select Market in accordance with Rule 103 of Regulation M under the Exchange Act during a period before the commencement of offers or sales of common stock and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, that bid must then be lowered when specified purchase limits are exceeded. Passive market making may cause the price of our common stock to be higher than the price that otherwise would exist in the open market in the absence of those transactions. The underwriters and dealers are not required to engage in passive market making and may end passive market making activities at any time.

Electronic Distribution

In connection with the offering, certain of the underwriters or securities dealers may distribute prospectuses by electronic means, such as e-mail.

Other Relationships

Some of the underwriters and their affiliates have engaged in, and may in the future engage in, investment banking and other commercial dealings in the ordinary course of business with us or our affiliates. They have received, or may in the future receive, customary fees and commissions for these transactions.

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In addition, in the ordinary course of their business activities, the underwriters and their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

A managing director of Leerink Partners LLC, one of the underwriters in this offering, has a 0.1% interest in Foresite Capital Fund I, L.P., who holds 1,585,743 shares of our common stock as of December 31, 2013.

Notice to Prospective Investors in the European Economic Area

In relation to each Member State of the European Economic Area (each, a "Relevant Member State"), no offer of shares may be made to the public in that Relevant Member State other than:

- A. to any legal entity which is a qualified investor as defined in the Prospectus Directive;
- B. to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives; or
- C. in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of shares shall require the Company or the representatives to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

Each person in a Relevant Member State who initially acquires any shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed that it is a "qualified investor" within the meaning of the law in that Relevant Member State implementing Article 2(1)(e) of the Prospectus Directive. In the case of any shares being offered to a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer of any shares to the public other than their offer or resale in a Relevant Member State to qualified investors as so defined or in circumstances in which the prior consent of the representatives has been obtained to each such proposed offer or resale.

The Company, the representatives and their affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

This prospectus has been prepared on the basis that any offer of shares in any Relevant Member State will be made pursuant to an exemption under the Prospectus Directive from the requirement to publish a prospectus for offers of shares. Accordingly any person making or intending to make an offer in that Relevant Member State of shares which are the subject of the offering contemplated in this prospectus may only do so in circumstances in which no obligation arises for the Company or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive in relation to such offer. Neither the Company nor the underwriters have authorized, nor do they authorize, the making of any offer of shares in circumstances in which an obligation arises for the Company or the underwriters to publish a prospectus for such offer.

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For the purpose of the above provisions, the expression "an offer to the public" in relation to any shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the shares to be offered so as to enable an investor to decide to purchase or subscribe the shares, as the same may be varied in the Relevant Member State by any measure implementing the Prospectus Directive in the Relevant Member State and the expression "Prospectus Directive" means Directive 2003/71/EC (including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member States) and includes any relevant implementing measure in the Relevant Member State and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

Notice to Prospective Investors in the United Kingdom

In addition, in the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are "qualified investors" (as defined in the Prospectus Directive) (i) who have professional experience in matters relating to investments falling within Article 19 (5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the "Order") and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as "relevant persons"). This document must not be acted on or relied on in the United Kingdom by persons who are not relevant persons. In the United Kingdom, any investment or investment activity to which this document relates is only available to, and will be engaged in with, relevant persons.

Notice to Prospective Investors in Switzerland

The shares may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange ("SIX") or on any other stock exchange or regulated trading facility in Switzerland. This document has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the shares or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, the Company or the shares have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA (FINMA), and the offer of shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes ("CISA"). The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of shares.

Notice to Prospective Investors in the Dubai International Financial Centre

This prospectus relates to an Exempt Offer in accordance with the Offered Securities Rules of the Dubai Financial Services Authority ("DFSA"). This prospectus is intended for distribution only to persons of a type specified in the Offered Securities Rules of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus nor taken steps to verify the information set forth herein and has no responsibility for the prospectus. The shares to which this prospectus relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the shares offered should conduct their own due diligence on the shares. If you do not understand the contents of this prospectus you should consult an authorized financial advisor.

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Notice to Prospective Investors in Australia

No placement document, prospectus, product disclosure statement or other disclosure document has been lodged with the Australian Securities and Investments Commission ("ASIC"), in relation to the offering. This prospectus does not constitute a prospectus, product disclosure statement or other disclosure document under the Corporations Act 2001 (the "Corporations Act"), and does not purport to include the information required for a prospectus, product disclosure statement or other disclosure document under the Corporations Act.

Any offer in Australia of the shares may only be made to persons (the "Exempt Investors") who are "sophisticated investors" (within the meaning of section 708(8) of the Corporations Act), "professional investors" (within the meaning of section 708(11) of the Corporations Act) or otherwise pursuant to one or more exemptions contained in section 708 of the Corporations Act so that it is lawful to offer the shares without disclosure to investors under Chapter 6D of the Corporations Act.

The shares applied for by Exempt Investors in Australia must not be offered for sale in Australia in the period of 12 months after the date of allotment under the offering, except in circumstances where disclosure to investors under Chapter 6D of the Corporations Act would not be required pursuant to an exemption under section 708 of the Corporations Act or otherwise or where the offer is pursuant to a disclosure document which complies with Chapter 6D of the Corporations Act. Any person acquiring shares must observe such Australian on-sale restrictions.

This prospectus contains general information only and does not take account of the investment objectives, financial situation or particular needs of any particular person. It does not contain any securities recommendations or financial product advice. Before making an investment decision, investors need to consider whether the information in this prospectus is appropriate to their needs, objectives and circumstances, and, if necessary, seek expert advice on those matters.

Notice to Prospective Investors in Hong Kong

The shares have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or (b) in other circumstances which do not result in the document being a "prospectus" as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of that Ordinance. No advertisement, invitation or document relating to the shares has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" as defined in the Securities and Futures Ordinance and any rules made under that Ordinance.

Notice to Prospective Investors in Japan

The shares have not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948, as amended) and, accordingly, will not be offered or sold, directly or indirectly, in Japan, or for the benefit of any Japanese Person or to others for re-offering or resale, directly or indirectly, in Japan or to any Japanese Person, except in compliance with all applicable laws, regulations and ministerial guidelines promulgated by relevant Japanese governmental or regulatory authorities in effect at the relevant time. For the purposes of this paragraph, "Japanese Person" shall mean any person resident in Japan, including any corporation or other entity organized under the laws of Japan.

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Notice to Prospective Investors in Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the "SFA"), (ii) to a relevant person pursuant to Section 275 (1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275, of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- (a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor,

securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares pursuant to an offer made under Section 275 of the SFA except:

- (a) to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;
- (b) where no consideration is or will be given for the transfer;
- (c) where the transfer is by operation of law;
- (d) as specified in Section 276(7) of the SFA; or
- (e) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

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LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed upon for us by Wilmer Cutler Pickering Hale and Dorr LLP, Boston, Massachusetts. Ropes & Gray LLP, Boston, Massachusetts, has acted as counsel for the underwriters in connection with certain legal matters related to this offering.

EXPERTS

The consolidated financial statements appearing in this Prospectus and Registration Statement have been audited by McGladrey LLP, an independent registered public accounting firm, as stated in their report appearing elsewhere herein, and are included in reliance upon such report and upon the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to the shares of common stock offered hereby. This prospectus, which constitutes a part of the registration statement, does not contain all of the information set forth in the registration statement or the exhibits and schedules filed therewith. For further information about us and the common stock offered hereby, we refer you to the registration statement and the exhibits and schedules filed therewith. Statements contained in this prospectus regarding the contents of any contract or any other document that is filed as an exhibit to the registration statement are not necessarily complete, and each such statement is qualified in all respects by reference to the full text of such contract or other document filed as an exhibit to the registration statement. We are required to file periodic reports, proxy statements, and other information with the SEC pursuant to the Exchange Act. You may read and copy this information at the SEC's public reference room, which is located at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You may obtain information on the operation of the public reference room by calling the SEC at 1-800-SEC-0330. The SEC also maintains an Internet website that contains reports, proxy statements and other information about registrants, like us, that file electronically with the SEC. The address of that site is www.sec.gov.

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**KARYOPHARM THERAPEUTICS INC.
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Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders
Karyopharm Therapeutics Inc.

We have audited the accompanying consolidated balance sheets of Karyopharm Therapeutics Inc. and subsidiaries (a development stage company) (the "Company") as of December 31, 2013 and 2012, and the related consolidated statements of operations, convertible preferred stock and stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2013, and for the period from December 22, 2008 (date of inception) through December 31, 2013. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of Karyopharm Therapeutics Inc. and subsidiaries as of December 31, 2013 and 2012, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2013, and from December 22, 2008 (date of inception) through December 31, 2013, in conformity with U.S. generally accepted accounting principles.

/s/ McGladrey LLP

Boston, Massachusetts
March 21, 2014

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Karyopharm Therapeutics Inc.
(A Development Stage Company)

Consolidated Balance Sheets

(in thousands, except share and per share data)

	December 31, 2013	December 31, 2012
ASSETS		
Current assets:		
Cash and cash equivalents (NPM restricted December 31, 2012 \$12)	\$ 155,974	\$ 391
Prepaid expenses and other current assets (NPM restricted December 31, 2012 \$485)	1,982	563
Total current assets	157,956	954
Property and equipment, net	240	327
Other assets	30	30
Total assets	\$ 158,226	\$ 1,311
LIABILITIES, CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)		
Current liabilities:		
Accounts payable (NPM restricted December 31, 2012 \$499)	\$ 1,740	\$ 1,076
Accrued expenses (NPM restricted December 31, 2012 \$312)	1,168	764
Deferred revenue	79	66
Other liabilities	305	24
Total current liabilities	3,292	1,930
Commitments and contingencies (Note 8)		
Preferred stock subscription		8,980
Convertible preferred stock		18,278
		27,258
Stockholders' equity (deficit):		
Common stock, \$0.0001 par value; 100,000,000 and 35,000,000 shares authorized at December 31, 2013 and 2012, respectively; 29,587,258 and 2,123,388 shares issued and outstanding at December 31, 2013 and 2012, respectively	3	
Preferred stock, \$0.0001 par value; 5,000,000 and no shares authorized at December 31, 2013 and 2012, respectively; no shares issued and outstanding		

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Additional paid-in capital	217,500	745
Deficit accumulated during the development stage	(62,569)	(28,622)
Total stockholders' equity (deficit)	154,934	(27,877)
Total liabilities, convertible preferred stock and stockholders' equity (deficit)	\$ 158,226	\$ 1,311

The accompanying notes are an integral part of these consolidated financial statements.

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Karyopharm Therapeutics Inc.
(A Development Stage Company)

Consolidated Statements of Operations

(in thousands, except share and per share data)

	For the Years Ended December 31,			Period from
	2013	2012	2011	December 22, 2008 (date of inception) to December 31, 2013
Contract and grant revenue	\$ 387	\$ 634	\$ 152	\$ 1,266
Operating expenses:				
Research and development	28,452	14,095	8,623	52,835
General and administrative	5,885	2,429	1,840	10,817
Total operating expenses	34,337	16,524	10,463	63,652
Loss from operations	(33,950)	(15,890)	(10,311)	(62,386)
Other income (expense):				
Interest income	3	2		5
Interest expense				(188)
Total other income (expense)	3	2		(183)
Net loss	\$ (33,947)	\$ (15,888)	\$ (10,311)	\$ (62,569)
Net loss per share applicable to common stockholders-basic and diluted	\$ (5.59)	\$ (8.95)	\$ (10.27)	\$ (35.00)
Weighted-average number of common shares outstanding used in net loss per share applicable to common stockholders-basic and diluted	6,067,679	1,775,323	1,004,144	1,787,668

The accompanying notes are an integral part of these consolidated financial statements.

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**Karyopharm Therapeutics Inc.
(A Development Stage Company)**

Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)

For the Period December 22, 2008 (date of inception) to December 31, 2013

(in thousands, except share and per share data)

	Special Participation Shares	Series A Convertible Preferred Shares	Series A Convertible Preferred Shares	Series A- Convertible Preferred Shares	Series B-1 Convertible Preferred Shares	Series B-1 Convertible Preferred Shares	Series B-1 Convertible Preferred Shares	Series B-1 Convertible Preferred Shares	Common Shares	Additional Paid- Capital	Deficit Accumulated During Development Stage	Total Shareholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Amount	Amount
Balance at December 22, 2008 (date of inception)		\$		\$		\$		\$		\$	\$	\$
Net loss												(179)
Balance at December 31, 2009												(179)
Proceeds from sale of restricted stock											1	1
Vesting of restricted stock								578,600				
Issuance of common stock in connection with a service agreement								151,515				
Issuance of Series A convertible preferred stock, net of issuance costs of \$160		5,000,000	4,840									
Issuance of special participation stock	10,000											
Conversion of notes payable into Series A convertible preferred stock		937,500	938									
Stock-based compensation expense										46		46
Net loss												(2,244)
Balance at December 31, 2010	10,000	5,937,500	5,778					730,115	47		(2,423)	(2,376)
Issuance of common stock in connection with a service								11,170				

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agreement			
Vesting of restricted stock			486,921
Issuance of Series A convertible preferred stock	5,000,000	5,000	
Proceeds from the sale of Series A-2 convertible preferred stock, net of issuance costs of \$35		6,100,000	6,980
Proceeds from sale of restricted stock to advisors			12
Stock-based compensation expense			24
Net loss			(10,311)

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6,100,000 6,980 1,764,706 3,000 1,538,461 2,000 1,000,000 2,000 (10,403,167) (13,980)

(20,937,500) (20,778) (6,100,000) (6,980) (1,764,706) (3,000) (1,538,461) (2,000) (24,100,000) (48,057) (8,636,362) (18,877) 19,114,241 2 9

12,121

79,122

438,386

7,820,000 1 11

29,587,258 3 21

The accompanying notes are an integral part of these consolidated financial statements.

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Karyopharm Therapeutics Inc.
(A Development Stage Company)

Consolidated Statements of Cash Flows

(in thousands)

	For the Year Ended December 31,			Period from
	2013	2012	2011	December 22, 2008 (date of inception) through December 31, 2013
Operating activities				
Net loss	\$ (33,947)	\$ (15,888)	\$ (10,311)	\$ (62,569)
Adjustments to reconcile net loss to net cash used in operating activities:				
Depreciation and amortization	144	122	83	350
Stock-based compensation	3,785	653	24	4,508
Noncash consulting expenses	88			788
Noncash interest expense on convertible notes				188
Change in operating assets and liabilities:				
Prepaid expenses and other current assets	(1,419)	(209)	(99)	(1,982)
Deposits				(30)
Accounts payable	664	(66)	1,131	1,740
Accrued expenses and other liabilities	382	13	423	1,170
Deferred revenue	13	(134)	200	79
 Net cash used in operating activities	 (30,290)	 (15,509)	 (8,549)	 (55,758)
Investing activities				
Purchases of property and equipment	(57)	(121)	(376)	(590)
 Net cash used in investing activities	 (57)	 (121)	 (376)	 (590)
Financing activities				
Proceeds of issuance of common stock, net of issuance costs	113,155	9	12	113,177
Proceeds from the exercise of stock options	341			341
Proceeds from issuance of convertible notes				250
Proceeds from issuance of preferred stock subscription		2,000	6,980	
Principal payments of convertible notes				(200)
Proceeds from sale of convertible preferred stock, net of issuance costs	72,434	7,500	5,000	98,754
 Net cash provided by financing activities	 185,930	 9,509	 11,992	 212,322
 Net increase (decrease) in cash and cash equivalents	 155,583	 (6,121)	 3,067	 155,974
Cash and cash equivalents, beginning of period	391	6,512	3,445	
 Cash and cash equivalents, end of period	 \$ 155,974	 \$ 391	 \$ 6,512	 \$ 155,974

Supplementary disclosure of noncash investing and financing activities:

Issuance of shares related to preferred stock subscription	\$	13,980	\$		\$		\$	13,980
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Preferred stock conversion to common stock	\$	99,691	\$		\$		\$	99,691
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Conversion of notes payable to preferred stock	\$		\$		\$		\$	750
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Issuance of convertible notes in satisfaction of accrued expenses	\$		\$		\$		\$	700
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The accompanying notes are an integral part of these consolidated financial statements.

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**Karyopharm Therapeutics Inc.
(A Development Stage Company)**

Notes to Consolidated Financial Statements

(in thousands, except share and per share data)

1. Organization and Operations

The Company

Karyopharm Therapeutics Inc., which we refer to as "Karyopharm" or the "Company", is a clinical stage pharmaceutical company that seeks to discover, develop, and commercialize drugs to treat cancer and other major diseases. It was incorporated in Delaware on December 22, 2008 and has a principal place of business in Natick, Massachusetts.

The Company's operations to date have consisted primarily of raising capital, product research and development, and initial market development. Accordingly, the Company is considered to be in the development stage at December 31, 2013. The Company's fiscal year ends on December 31.

The Company has not generated any revenue related to its primary business purpose to date and is subject to a number of risks similar to those of other development stage life science companies, including dependence on key individuals, competition from other companies, the need for development of commercially viable products, and the need to obtain adequate additional financing to fund the development of its product candidates. The Company is also subject to a number of risks similar to other companies in the industry, including rapid technological change, regulatory approval of products, uncertainty of market acceptance of products, competition from substitute products and larger companies, the need to obtain additional financing, compliance with government regulations, protection of proprietary technology, dependence on third parties, product liability and dependence on key individuals.

The Company has generated an accumulated deficit of \$62.6 million since inception. The Company has financed its operations primarily through private placements of its preferred stock and an initial public offering ("IPO") completed in 2013. The Company has not completed development of any product candidate and has devoted substantially all of its financial resources and efforts to research and development, including preclinical and clinical development. The Company expects to continue to incur significant expenses and increasing operating losses for at least several years.

Initial public offering

In November 2013, the Company closed its IPO of its common stock, which resulted in the sale of 6,800,000 shares of its common stock at a public offering price of \$16.00 per share. In December 2013, the Company issued 1,020,000 shares of common stock upon the exercise by the underwriters of their option to purchase additional shares at the public offering price. The Company received net proceeds from the IPO of approximately \$113.2 million, after deducting underwriting discounts and expenses payable by the Company.

In connection with preparing for the IPO, the Company's Board of Directors and stockholders approved a one-for-3.3 reverse stock split of the Company's common stock. The reverse stock split became effective in October 2013. All share and per share amounts in the consolidated financial statements and notes thereto have been retroactively adjusted for all periods presented to give effect to this reverse stock split, including reclassifying an amount equal to the reduction in par value of common stock to additional paid-in capital.

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**Karyopharm Therapeutics Inc.
(A Development Stage Company)**

Notes to Consolidated Financial Statements (Continued)

(in thousands, except share and per share data)

1. Organization and Operations (Continued)

In connection with the closing of the IPO, all of the Company's outstanding convertible preferred stock automatically converted to common stock in November 2013, resulting in an additional 19,114,241 shares of common stock of the Company becoming outstanding. The significant increase in common stock outstanding in November 2013 is expected to impact the year-over-year comparability of the Company's net loss per share calculations in future periods.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("U.S. GAAP").

Segment Information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one operating segment, which is the business of discovering, developing and commercializing drugs to treat cancer and other major diseases. All of the Company's revenues are derived in the United States. All material long-lived assets of the Company reside in the United States.

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period.

On an ongoing basis, the Company's management evaluates its estimates, including estimates related to clinical trial accruals, stock-based compensation expense, and reported amounts of revenues and expenses during the reported period. The Company bases its estimates on historical experience and other market-specific or other relevant assumptions that it believes to be reasonable under the circumstances. Although the Company regularly assesses these estimates, actual results could differ from those estimates. Changes in estimates are recorded in the period in which they become known.

Principles of Consolidation

The consolidated financial statements include the accounts of Karyopharm Therapeutics Inc. (a Delaware corporation) as well as the accounts of Karyopharm Securities Corp. ("KPSC", a Massachusetts corporation), incorporated in December 2013, and NPM Pharma Inc. ("NPM", a Canadian corporation), two wholly-owned subsidiaries requiring consolidation. All significant intercompany balances and transactions have been eliminated in consolidation.

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Karyopharm Therapeutics Inc.
(A Development Stage Company)

Notes to Consolidated Financial Statements (Continued)

(in thousands, except share and per share data)

2. Summary of Significant Accounting Policies (Continued)

NPM was formed in December 2011 and was 50% owned by the Company until it became a wholly-owned subsidiary in August 2013. NPM was established to procure research and development services in connection with clinical pharmaceutical studies with Canadian vendors on the Company's behalf.

A Variable Interest Entity ("VIE") is an entity that either (i) has insufficient equity to permit the entity to finance its activities without additional subordinated financial support or (ii) has equity investors who lack the characteristics of a controlling financial interest. A VIE is consolidated by its primary beneficiary. The primary beneficiary has both the power to direct the activities that most significantly impact the entity's economic performance and the obligation to absorb losses or the right to receive benefits from the entity that could potentially be significant to the VIE. Prior to August 2013, NPM was a VIE, and the Company, as its primary beneficiary, presented consolidated financials that included the accounts of NPM at December 31, 2012.

Total NPM assets and liabilities reflected on the Company's balance sheet for December 31, 2012 are as follows:

		December 31, 2012
Assets:		
Cash and Cash Equivalents	\$	12
Prepaid Expenses and other current assets		485
Total Assets	\$	497
Liabilities:		
Accounts payable	\$	499
Accrued expenses and other liabilities		312
Total Liabilities	\$	811

Cash and Cash Equivalents

Cash equivalents consist primarily of demand deposit accounts and deposits in short-term money market funds. Cash equivalents are stated at cost, which approximates fair market value. The Company considers all highly liquid investments with maturities of three months or less from the date of purchase to be cash equivalents.

Concentrations of Credit Risk and Off-Balance Sheet Risk

Financial instruments which potentially subject the Company to concentrations of credit risk consist principally of cash and cash equivalents. The Company maintains cash accounts in commercial banks, which may, at times, exceed federally insured limits. The Company

has not experienced any losses in such accounts. The Company believes it is not exposed to any significant credit risk on cash and cash equivalents.

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Karyopharm Therapeutics Inc.
(A Development Stage Company)

Notes to Consolidated Financial Statements (Continued)

(in thousands, except share and per share data)

2. Summary of Significant Accounting Policies (Continued)

Fair Value Measurements

The Company's financial instruments consist principally of cash and cash equivalents, accounts payable, and accrued liabilities. Fair value measurements are classified and disclosed in one of the following three categories:

Level 1 Quoted prices in active markets for identical assets or liabilities.

Level 2 Inputs other than Level 1 that are observable, either directly or indirectly, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3 Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

Assets and liabilities measured at fair value on a recurring basis as of December 31, 2013 and 2012 are as follows:

Description	Balance as of December 31, 2013	Fair Value Measurements at Reporting Date Using		
		Level 1	Level 2	Level 3
Money Market Funds, included in cash equivalents	\$ 155,765	\$	\$ 155,765	\$

Description	Balance as of December 31, 2012	Fair Value Measurements at Reporting Date Using		
		Level 1	Level 2	Level 3
Money Market Funds, included in cash equivalents	\$ 2	\$	\$ 2	\$

The cash equivalents represent deposits in a short term money market fund. The Company measures cash equivalents at fair value on a recurring basis. The fair value of cash equivalents is determined based on "Level 2" inputs.

Property and Equipment, net

Property and equipment are recorded at cost, less accumulated depreciation. Depreciation is recorded using the straight-line method over the estimated useful lives of the respective assets, generally three to five years. Leasehold improvements are amortized over the shorter of the lease term or the estimated useful economic lives of the related assets. Expenditures for maintenance and repairs are charged to expense

while the costs of significant improvements are capitalized. Upon retirement or sale, the cost of the assets disposed of and the related accumulated depreciation are eliminated from the balance sheets and any related gains or losses are reflected in the consolidated statements of operations.

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**Karyopharm Therapeutics Inc.
(A Development Stage Company)**

Notes to Consolidated Financial Statements (Continued)

(in thousands, except share and per share data)

2. Summary of Significant Accounting Policies (Continued)

Long-Lived Assets

The Company reviews the carrying values of its long-lived assets for possible impairment whenever events or changes in circumstances indicate that the carrying amounts of the assets may not be recoverable. Any long-lived assets held for disposal are reported at the lower of their carrying amounts or fair values less costs to sell. The Company has not recorded an impairment in any period since inception.

Revenue Recognition

The Company recognizes revenue in accordance with Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("ASC") Topic 605, *Revenue Recognition*. The Company recognizes revenue in accordance with the milestone method of revenue recognition for arrangements involving research or development or other performance obligations whereby a portion or all of the consideration is contingent upon achievement of milestone events. Under these provisions, arrangement consideration contingent upon achievement of a milestone is recognized by the Company in the period the milestone is met when the Company concludes that the milestone is substantive. At the inception of each applicable arrangement, the Company assesses each milestone and the consideration payable upon achievement of each milestone and concludes that the milestone is substantive if all of the following criteria are met: (i) the consideration is commensurate with the Company's performance or the enhanced value of a delivered item which is a direct result of the Company's performance to achieve the milestone, (ii) the consideration relates to past performance and there are no refund rights or other penalties related to the consideration based on completion of future performance and (iii) the consideration is reasonable relative to all the deliverables and payment terms within the arrangement. The related consideration for milestones that are considered substantive is recognized in its entirety in the period which the milestone is met.

The milestone method of revenue recognition was applicable to two research agreements which were executed during 2013 and 2011, respectively.

The agreement executed during 2013 includes payments upon the achievement of several development milestones as well as an upfront payment. The Company concluded that the upfront payment of \$100 did not represent a substantive milestone. Accordingly, the Company is recognizing this amount on a straight-line basis from the date when substantive services commenced through the estimated completion of the final milestone. As of December 31, 2013, no additional milestones were met according to this research agreement. During the year ended December 31, 2013, the Company recognized \$21 of the upfront payment pursuant to this research agreement.

The agreement executed during 2011 includes payments upon the achievement of several development milestones as well as an upfront payment. The Company concluded that the upfront payment of \$200 did not represent a substantive milestone. Accordingly, the Company recognized this amount on a straight-line basis from the date when substantive services commenced through the estimated completion of the final milestone. As of December 31, 2011, none of the milestones had been met and no revenue was recognized. During the year ended December 31, 2012, the Company recognized \$634 related to this research agreement, including \$134 of the upfront payment. During the

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**Karyopharm Therapeutics Inc.
(A Development Stage Company)**

Notes to Consolidated Financial Statements (Continued)

(in thousands, except share and per share data)

2. Summary of Significant Accounting Policies (Continued)

year ended December 31, 2013, the Company recognized \$366 related to this agreement, including \$66 related to the upfront payment and \$300 related to other milestones associated with the agreement. For the period from December 22, 2008 (date of inception) to December 31, 2013, the Company recognized revenue of \$1.0 million under this research agreement. There are no future milestones to be met under this agreement.

During 2010, the Company was awarded a federal grant in the amount of \$245 under the Qualifying Therapeutic Discovery Project ("QTDP") related to research performed in 2009 and 2010 of which \$93 and \$152 was received and recognized in income during the years ended December 31, 2010 and December 31, 2011, respectively. For the period from December 22, 2008 (date of inception) to December 31, 2013, the Company recognized revenue of \$245 related to the QTDP.

Organizational Costs

All organizational costs are expensed as incurred.

Research and Development Expenses

Research and development costs are charged to expense as incurred and include, but are not limited to:

employee-related expenses, including salaries, benefits, travel and stock-based compensation expense;

expenses incurred under agreements with contract research organizations, contract manufacturing organizations and consultants that conduct clinical trials and preclinical studies;

the cost of acquiring, developing and manufacturing clinical trial materials;

facility, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and other supplies; and

costs associated with preclinical activities and regulatory operations.

Costs for certain development activities, such as clinical trials, are recognized based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations, or information provided to the Company by its vendors on their actual costs incurred. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the financial statements as prepaid or accrued research and development.

Comprehensive Loss

Comprehensive loss consists of net loss and changes in equity during a period from transactions and other equity and circumstances generated from non-owner sources. The Company's net loss equals comprehensive loss for all periods presented.

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**Karyopharm Therapeutics Inc.
(A Development Stage Company)**

Notes to Consolidated Financial Statements (Continued)

(in thousands, except share and per share data)

2. Summary of Significant Accounting Policies (Continued)

Income Taxes

The Company uses the liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on the difference between the financial reporting and the tax reporting basis of assets and liabilities and are measured using the enacted tax rates and laws that are expected to be in effect when the differences are expected to reverse. The Company provides a valuation allowance against net deferred tax assets unless, based upon the available evidence, it is more likely than not that the deferred tax assets will be realized. The Company has evaluated available evidence and concluded that the Company may not realize the benefit of its deferred tax assets; therefore a valuation allowance has been established for the full amount of the deferred tax assets. The Company's practice is to recognize interest and/or penalties related to income tax matters in income tax expense.

Accounting for Stock-Based Compensation

The Company accounts for its stock-based compensation awards in accordance with FASB ASC Topic 718, *Compensation Stock Compensation* ("ASC 718"). ASC 718 requires all stock-based payments to employees, including grants of employee stock options and restricted stock and modifications to existing stock options, to be recognized in the consolidated statements of operations and comprehensive loss based on their fair values. The Company uses the Black-Scholes option pricing model to determine the fair value of options granted.

Consistent with the guidance in FASB ASC Topic 505-50, *Equity-Based Payments to Non-Employees*, the fair value of each non-employee stock option is estimated at the date of grant using the Black-Scholes option pricing model with assumptions generally consistent with those used for employee stock options, with the exception of expected term, which is over the contractual life.

Compensation expense related to awards to employees is recognized on a straight-line basis based on the grant date fair value over the associated service period of the award, which is generally the vesting term. Awards to non-employees are adjusted through stock-based compensation expense as the award vests to reflect the current fair value of such awards, and expensed using an accelerated attribution model.

Net Loss Per Share

Basic net loss per share is computed by dividing net loss by the weighted average number of common shares outstanding for the period. The Company's potential dilutive shares, which include outstanding common stock options and unvested restricted stock, have not been included in the computation of diluted net loss per share for any of the periods presented as the result would be antidilutive.

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Karyopharm Therapeutics Inc.
(A Development Stage Company)

Notes to Consolidated Financial Statements (Continued)

(in thousands, except share and per share data)

2. Summary of Significant Accounting Policies (Continued)

The amounts in the table below were excluded from the calculation of diluted weighted-average shares outstanding, prior to the use of the treasury stock method, due to their anti-dilutive effect:

	December 31,		Period from December 22, 2008 (date of inception) to December 31, 2013.	
	2013	2012	2011	
Convertible preferred stock		5,587,121	3,314,393	
Special participation stock		10,000	10,000	
Outstanding stock options	2,410,518	691,367	1,086,221	2,410,518
Non-vested restricted stock	166,949	541,218	938,143	166,949

3. Property and Equipment, net

Property and equipment, net consist of the following:

	Estimated Useful Life Years	December 31,	
		2013	2012
Laboratory Equipment	4	\$ 328	\$ 314
Furniture and fixtures	5	98	90
Office and computer equipment	3	85	85
Leasehold improvements	Lease Term	79	44
		590	533
Less accumulated depreciation and amortization		(350)	(206)
Property and equipment, net		\$ 240	\$ 327

Depreciation and amortization expense recorded for the years ended December 31, 2013, 2012, and 2011 were \$144, \$122, and \$83, respectively. Depreciation and amortization expense for the period from December 22, 2008 (date of inception) to December 31, 2013 was \$350.

4. Research Agreements

In July 2011 and September 2013, the Company entered into research agreements in which the Company received payments upon the achievement of certain milestones. The agreements require the Company to pay royalties on product sales, up to a predetermined maximum. The Company must also pay a royalty on any sublicense income, up to a predetermined maximum. From the period December 22, 2008 (date of inception) to December 31, 2013, no royalties or sublicense payments have been made.

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Karyopharm Therapeutics Inc.
(A Development Stage Company)

Notes to Consolidated Financial Statements (Continued)

(in thousands, except share and per share data)

5. Accrued Liabilities

Accrued expenses consist of the following:

(in thousands)	December 31,	
	2013	2012
Payroll and employee-related costs	\$ 100	\$ 302
Research and development costs	698	333
Professional	215	
Other	155	129
Total Accrued Expenses	\$ 1,168	\$ 764

6. Related Party Transactions

The company incurred expenses for consulting and contract research services with certain related parties, including a family member of management and a board member, of \$418, \$109, \$889, and \$1,416 for the years ended December 31, 2013, 2012, 2011 and the period from December 22, 2008 (date of inception) through December 31, 2013. There are no amounts included in accounts payable or accrued expenses at December 31, 2013, 2012 or 2011 due to related parties.

7. Stockholders' Equity***Common Stock***

In November 2013, the Company closed an IPO of its common stock, which resulted in the sale of 6,800,000 shares of its common stock at a public offering price of \$16.00 per share. In December 2013, the Company issued 1,020,000 shares of common stock upon the exercise by the underwriters of their option to purchase additional shares at the public offering price. The Company received net proceeds from the IPO of approximately \$113.2 million, after deducting underwriting discounts and expenses payable by the Company.

In connection with preparing for the IPO, the Company's Board of Directors and stockholders approved a one-for-3.3 reverse stock split of the Company's common stock. The reverse stock split became effective in October 2013. All share and per share amounts in the consolidated financial statements and notes thereto have been retroactively adjusted for all periods presented to give effect to this reverse stock split, including reclassifying an amount equal to the reduction in par value of common stock to additional paid-in capital.

In connection with the closing of the IPO, all of the Company's outstanding convertible preferred stock automatically converted to common stock in November 2013, resulting in an additional 19,114,241 shares of common stock of the Company becoming outstanding. The significant increase in common stock outstanding in November 2013 is expected to impact the year-over-year comparability of the Company's net loss per share calculations in future periods.

In October 2010, the Company issued and sold 1,958,210 shares of its common stock, subject to restrictions that vest over time, to the founders of the Company for an aggregate cash consideration of \$1. In October 2010, the Company entered into a service contract and, pursuant to the terms of such contract, the Company was obligated to issue shares. The Company issued 162,685 shares of common

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Karyopharm Therapeutics Inc.
(A Development Stage Company)

Notes to Consolidated Financial Statements (Continued)

(in thousands, except share and per share data)

7. Stockholders' Equity (Continued)

stock in connection with this service contract. In December 2011, the Company issued and sold 45,454 shares of its common stock, subject to restrictions that vest over time, to two advisors of the Company for an aggregate cash consideration of \$12. In accordance with the terms of the restricted stock agreements, the Company has the right (but not an obligation) to repurchase, at the original purchase price, any non-vested shares of the restricted common stock in the event of termination of the business relationship. Restricted shares are recorded as outstanding as they vest. There were 541,218 and 166,949 shares of non-vested restricted common stock at December 31, 2012 and December 31, 2013, respectively.

Preferred Stock

The Company's convertible preferred stock consisted of the following as of December 31, 2013 and 2012:

	As of December 31,	
	2013	2012
Series A convertible preferred stock, \$0.0001 par value; Authorized-no shares and 20,937,500 at December 31, 2013 and 2012, respectively; Issued and outstanding-no shares and 18,437,500 at December 31, 2013 and 2012, respectively	\$	\$18,278
Series A-2 convertible preferred stock, \$0.0001 par value; Authorized, issued and outstanding-no shares at December 31, 2013 and 2012		
Series A-3 convertible preferred stock, \$0.0001 par value; Authorized, issued and outstanding-no shares at December 31, 2013 and 2012		
Series A-4 convertible preferred stock, \$0.0001 par value; Authorized, issued and outstanding-no shares at December 31, 2013 and 2012		
Series B convertible preferred stock, \$0.0001 par value; Authorized, issued and outstanding-no shares at December 31, 2013 and 2012		
Series B-1 convertible preferred stock, \$0.0001 par value; Authorized, issued and outstanding-no shares at December 31, 2013 and 2012		
	\$	\$18,278

In October of 2010, the Company entered into an agreement to issue and sell 20,000,000 shares of Series A Preferred Stock at \$1.00 per share, which was effectuated in two tranches. The first closing of the first tranche occurred in October 2010, in which the Company issued and sold 5,000,000 shares of Series A Preferred Stock for gross proceeds of \$5.0 million. The remaining 5,000,000 shares of the first tranche were issued and sold in 2011 for gross proceeds of \$5.0 million. In accordance with the terms of the Series A Preferred Stock Purchase Agreement, the Company issued and sold an additional 10,000,000 shares of Series A Preferred Stock in the second tranche, of which 2,500,000 shares were sold upon the achievement of a pre-defined milestone, and 2,500,000 shares were sold in

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**Karyopharm Therapeutics Inc.
(A Development Stage Company)**

Notes to Consolidated Financial Statements (Continued)

(in thousands, except share and per share data)

7. Stockholders' Equity (Continued)

each of the following three calendar quarters, for total cash consideration of \$10.0 million. As discussed below, the Company met this milestone in June 2012.

In connection with the sale of Series A Preferred Stock, in October 2010, outstanding convertible notes in the amount of \$750 were converted into 937,500 shares of Series A Preferred Stock with a value of \$938. The difference between the carrying value of the convertible notes and the fair value of the shares issued pursuant to the contractual terms of the conversion of \$188 was recorded as a beneficial conversion feature in 2010.

On October 31, 2011, the Company entered into a stock purchase agreement with an existing stockholder for the purpose of issuing and selling up to 7,000,000 shares of Series A-2 Preferred Stock and the sale of up to 3,000,000 shares of Series A-3 Preferred Stock in two closings.

Pursuant to this agreement, the Company agreed to sell 6,100,000 shares of Series A-2 Preferred Stock at \$1.15 per share for gross proceeds of \$7.0 million. The Company accounted for this stock purchase as a preferred stock subscription as these shares were not issued until August 2013.

Upon meeting a pre-defined clinical milestone in February 2013, the Company agreed to sell 1,764,706 shares of Series A-3 Preferred Stock at \$1.70 per share for gross proceeds of \$3.0 million. The Company accounted for this stock purchase as a preferred stock subscription as these shares were not issued until August 2013.

In February 2012, the Company agreed to sell 1,538,461 shares of Series A-4 Preferred Stock at \$1.30 per share for gross proceeds of \$2.0 million. The Company accounted for this stock purchase as a preferred stock subscription as these shares were not issued until August 2013.

In June 2012, the Company achieved the milestone for the second tranche of the Series A Preferred Stock Agreement. In accordance with the terms of the Agreement, the Company sold 2,500,000 shares of Series A Preferred Stock in June 2012 for \$2.5 million and sold 2,500,000 shares of Series A Preferred Stock in each of the following three calendar quarters.

Between April and July 2013, the Company issued and sold an aggregate of 11,600,000 shares of Series B Preferred Stock at a price per share of \$2.00 for an aggregate purchase price of \$23.2 million. Upon the earlier of (i) September 6, 2013 or (ii) immediately prior to the closing of a firm commitment underwritten initial public offering of the Company's securities pursuant to an effective registration statement filed with the SEC, certain of the Company's existing investors were obligated to purchase an additional 12,500,000 shares of the Company's Series B Preferred Stock at a price per share of \$2.00, for gross proceeds of \$25.0 million. Such shares were issued in September 2013.

In July 2013, the Company issued and sold an aggregate of 8,636,362 shares of Series B-1 Preferred Stock at a price per share of \$2.20 for gross proceeds of \$19.0 million.

In August 2013, the Company issued (i) an aggregate of 6,100,000 shares of its series A-2 preferred stock at a purchase price per share of \$1.15, for an aggregate purchase price of \$7,015,000, (ii) an aggregate of 1,764,706 shares of its series A-3 preferred stock at a purchase price per share of \$1.70, for an aggregate purchase price of \$3,000,000, and (iii) an aggregate of 1,538,461 shares of its

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**Karyopharm Therapeutics Inc.
(A Development Stage Company)**

Notes to Consolidated Financial Statements (Continued)

(in thousands, except share and per share data)

7. Stockholders' Equity (Continued)

series A-4 preferred stock, at a purchase price per share of \$1.30, for an aggregate purchase price of \$1,999,999.

The Company has evaluated the tranching nature of certain of its Preferred Stock financings, as well as its rights, preferences and privileges of each series of Preferred Stock and has concluded that there are no freestanding derivative instruments, embedded derivatives requiring bifurcation, or any beneficial conversion features. All issued and subscribed shares of Preferred Stock are classified outside of Stockholder's Equity (Deficit) due to the presence of deemed liquidation provisions in the underlying agreements. Proceeds received relating to the sale of Series A-2, A-3, A-4 and B Preferred Stock were classified as a subscription until the shares were delivered in August 2013.

The Preferred Stockholders were entitled to certain conversion, dividend, voting and liquidation rights.

In connection with the closing of the IPO, all of the Company's outstanding convertible preferred stock automatically converted to common stock in November 2013, resulting in an additional 19,114,241 shares of common stock of the Company becoming outstanding. Upon the closing of its IPO, the Company had 5,000,000 shares of authorized preferred stock. As of December 31, 2013, the Company does not have any preferred stock issued or outstanding.

Special Participation Stock

Upon the sale of Series A Preferred Stock, the Company amended various restricted stock agreements to allow for the sale and issuance of 10,000 shares of special participation stock ("Special Participation Stock") for \$0.0001 per share (par value) for nominal consideration. The fair value of these shares during 2011 and 2012 was immaterial. In accordance with the terms of the amended restricted stock agreements, the Company has the right (but not an obligation) to repurchase, at the original purchase price, any unvested shares of Special Participation Stock in the event of termination of the underlying business relationship. There were 4,556 and 2,071 shares of unvested Special Participation Stock at December 31, 2011 and 2012, respectively.

In July 2013, the Company issued 12,121 shares of common stock in settlement of all outstanding shares of Special Participation Stock. There are no outstanding shares of Special Participation Stock at December 31, 2013.

8. Commitments and Contingencies

Operating Leases

The Company leases its facility under an operating lease that expires in January 2015. In January 2012 and July 2013, the Company amended its operating lease to increase the rentable square footage. The Company has the option to renew the lease for an additional two year option at then current market rate which may include escalations in rent payments during the new term. The Company recognizes rent expense on a straight-line basis over the non-cancelable lease term.

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Karyopharm Therapeutics Inc.
(A Development Stage Company)

Notes to Consolidated Financial Statements (Continued)

(in thousands, except share and per share data)

8. Commitments and Contingencies (Continued)

As of December 31, 2013, the minimum future rent payments under the lease agreement are as follows:

2014	\$ 98
2015	8
Total future minimum lease payments	\$ 106

The Company recorded rent expense totaling \$174, \$127, and \$70 for the periods ending December 31, 2013, 2012, and 2011, respectively, and \$375 for the period from December 22, 2008 (date of inception) to December 31, 2013.

Litigation

From time to time the Company may face legal claims or actions in the normal course of business. The Company is not currently a party to any litigation and, accordingly, does not have amounts recorded for any litigation-related matters.

9. Stock-based Compensation

During 2010, the Company established the 2010 Stock Incentive Plan (the "Plan" or the "2010 Plan"). As of December 31, 2013, the Company can issue a maximum number of 1,878,416 shares under the Plan pursuant to outstanding stock options. Under the terms of the Plan, options and other equity interests may be granted to employees, officers, directors, consultants and advisors of the Company. The exercise price of each stock option shall be the fair market value as determined in good faith by the Board of Directors (the Board) at the time each option is granted. The Company has granted service-based options under the Plan. Service-based option grants under the Plan generally vest as follows: 25% of the shares vest one calendar year from the vesting start date, 2.083% of the shares vest on the first day of each month thereafter. The options granted under the Plan generally expire in 10 years.

In October 2013, the Company's board of directors adopted and the Company's stockholders approved the 2013 Stock Incentive Plan (the "2013 Plan"). The 2013 Plan became effective immediately prior to the closing of the IPO and provides for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock unit awards and other stock-based awards. The number of shares of Common Stock reserved for issuance under the 2013 Plan is equal to the sum of (1) 969,696 shares plus (2) the number of shares (up to 2,126,377 shares) equal to the sum of the number of shares of Common Stock then available for issuance under the 2010 Plan and the number of shares of Common Stock subject to outstanding awards under the 2010 Plan that expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by the Company at their original issuance price pursuant to a contractual repurchase right plus (3) an annual increase, to be added on the first day of each fiscal year, beginning with the fiscal year ending December 31, 2014 and continuing until, and including, the fiscal year ending December 31, 2023, equal to the least of (A) 1,939,393 shares of Common Stock, (B) 4% of the number of shares of Common Stock outstanding on the first day of such fiscal year, and (C) an amount

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Karyopharm Therapeutics Inc.
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Notes to Consolidated Financial Statements (Continued)

(in thousands, except share and per share data)

9. Stock-based Compensation (Continued)

determined by the Company's board of directors. The Company will grant no further stock options or other awards under the 2010 Plan.

In connection with all share-based payment awards, total stock-based compensation expense recognized is as follows:

	Year Ended December 31,			Period from December 22, 2008 (date of inception) to December 31,
	2011	2012	2013	2013
Research and development	\$ 24	\$ 605	\$ 2,567	\$ 3,242
General and administrative		\$ 48	\$ 1,218	\$ 1,266
Total	\$ 24	\$ 653	\$ 3,785	\$ 4,508

Stock Options

Total expense related to employee and non-employee stock options for the years ended December 31, 2011, 2012 and 2013, and the period from December 22, 2008 (date of inception) to December 31, 2013 was \$17, \$264, \$3,020 and \$3,307, respectively.

The following table summarizes stock option activity for employees and nonemployees:

	Shares	Weighted- Average Exercise Price	Weighted- Average Remaining Contractual Term (years)	Aggregate Intrinsic Value
Options outstanding at December 31, 2012	691,367	\$ 0.46	8.8	\$ 1,666
Granted	1,914,195	\$ 9.94		
Exercised(1)	(142,758)	\$ 2.36		
Forfeited	(52,282)	\$ 1.73		
Options outstanding at December 31, 2013	2,410,522	\$ 7.85	9.3	\$ 36,717
Options vested or expected to vest at December 31, 2013(2)	2,269,359	\$ 8.10	9.3	\$ 34,002

Options exercisable at December 31, 2013	317,804	\$	0.34	7.5	\$	7,177
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- (1) Exercises include the issuance of 63,636 shares of non-vested restricted stock pursuant to the exercise of stock options prior to vesting. The Company has the right to repurchase the unvested shares under certain circumstances.
- (2) This represents the number of vested options, plus the number of unvested options that the Company estimated would vest, based on the unvested options as of the year ended December 31, 2013 as adjusted for the estimated forfeiture rate.

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Karyopharm Therapeutics Inc.
(A Development Stage Company)

Notes to Consolidated Financial Statements (Continued)

(in thousands, except share and per share data)

9. Stock-based Compensation (Continued)

The total intrinsic value of stock options exercised in the years ended December 31, 2011, 2012 and 2013 and for the period December 22, 2008 (date of inception) to December 31, 2013 was \$ 0, \$115, \$239, and \$354, respectively.

The Company estimates the fair value of each employee and non-employee stock award on the grant date using the Black-Scholes option-pricing model based on the following assumptions:

	Years Ended December 31,		
	2013	2012	2011
Volatility	85%-93%	79%-92%	78%-79%
Expected term (in years)	6.25-10	6.25-10	6.25-10
Risk-free interest rate	1.07%-3.01%	0.85%-1.76%	1.18%-2.62%
Dividend	0%	0%	0%

The Company uses the simplified method as prescribed by the Securities and Exchange Commission Staff Accounting Bulletin No. 107, *Share-Based Payment*, to calculate the expected term as it does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term for options granted to employees and utilizes the contractual term for options granted to non-employees. The expected term is applied to the stock option grant group as a whole, as the Company does not expect substantially different exercise or post-vesting termination behavior among its employee population. The computation of expected volatility is based on the historical volatility of a representative group of companies with similar characteristics to the Company, including early stage of product development and therapeutic focus. The risk-free interest rate is based on a treasury instrument whose term is consistent with the expected term of the stock options. Management estimates expected forfeitures based on data from a representative group of companies with similar characteristics to the Company and recognizes compensation costs only for those equity awards expected to vest.

Using the Black-Scholes option-pricing model, the weighted-average grant date fair values of options granted during the years ended December 31, 2011, 2012 and 2013, and the period from December 22, 2008 (date of inception) to December 31, 2013 was \$0.10, \$1.19, \$11.09, and \$7.05 per share, respectively.

As of December 31, 2012 and December 31, 2013, there was \$351 and \$21.0 million, respectively, of total unrecognized compensation cost related to employee and non-employee unvested stock options granted under the Plan and the 2013 Plan. The total unrecognized compensation cost will be adjusted for future forfeitures. As of December 31, 2013, the Company expects to recognize that cost over a remaining weighted-average period of 3.7 years.

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Karyopharm Therapeutics Inc.
(A Development Stage Company)

Notes to Consolidated Financial Statements (Continued)

(in thousands, except share and per share data)

9. Stock-based Compensation (Continued)

Restricted Stock

To date, the Company has granted 1,958,210 shares of restricted stock outside of the Plan and the 2013 Plan and 45,454 shares of restricted stock under the Plan. The following table summarizes the status of the Company's non-vested restricted common shares:

	Number of Shares	Weighted-Average Grant Date Fair Value
Non-vested at December 31, 2012	362,596	\$ 0.04
Granted		
Cancelled		
Vested	(352,652)	0.04
Non-vested at December 31, 2013(1)	9,943	\$ 0.26

(1) Excludes 157,006 shares of non-vested restricted stock remaining from the early exercise of stock options as of December 31, 2013.

The total expense related to employee and non-employee restricted stock for the years ended December 31, 2011, 2012, 2013, and the period from December 22, 2008 (date of inception) to December 31, 2013 was \$7, \$389, \$765 and \$1,201.

As of December 31, 2012, and December 31, 2013, there was \$380 and \$228, respectively, of total unrecognized compensation cost related to employee and non-employee non-vested restricted stock. As of December 31, 2013, the unrecognized expense is expected to be recognized over a weighted average period of 1.7 years.

10. Income Taxes

The Company provides for income taxes under ASC Topic 740, Accounting for Income Taxes. Under ASC Topic 740, the liability method is used in accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on differences between financial reporting and tax bases of assets and liabilities, and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse.

For the years ended December 31, 2013 and 2012, the Company did not record a current or deferred income tax expense or benefit.

The components of income (loss) before income taxes were as follows:

Year ended December 31,	
2013	2012

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Foreign	(10,922)	
U.S.	(23,025)	(15,888)
Totals	\$ (33,947)	\$ (15,888)

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Karyopharm Therapeutics Inc.
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Notes to Consolidated Financial Statements (Continued)

(in thousands, except share and per share data)

10. Income Taxes (Continued)

Deferred taxes are recognized for temporary differences between the basis of assets and liabilities for financial statement and income tax purposes. The significant components of the Company's deferred tax assets are comprised of the following:

	Year ended December 31,	
	2013	2012
Deferred tax assets:		
U.S. and state net operating loss carryforwards	\$ 17,876	\$ 10,621
Foreign net operating loss carryforwards	2,731	
Research and development credits	2,670	871
Accruals and other temporary differences	1,819	335
Total deferred tax assets	25,096	11,827
Less valuation allowance	(25,096)	(11,827)
Net deferred tax assets	\$	\$

The Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets. Based on the Company's history of operating losses, the Company has concluded that it is more likely than not that the benefit of its deferred tax assets will not be realized. Accordingly, the Company has provided a full valuation allowance for deferred tax assets as of December 31, 2013 and 2012. The valuation allowance increased approximately \$13.3 million and \$6.2 million during the years ended December 31, 2013 and 2012, respectively, due primarily to the generation of net operating losses during the periods then ended.

A reconciliation of income tax expense computed at the statutory federal income tax rate to income taxes as reflected in the financial statements is as follows:

	Year ended December 31,	
	2013	2012
Federal income tax expense at statutory rate	34.0%	34.0%
State income tax, net of federal benefit	4.9%	5.2%
Permanent differences	0.0%	(0.1)%
Research and development credit	3.9%	0.0%
Foreign rate differential	(2.9)%	0.0%
Other	(0.8)%	(0.0)%
Change in valuation allowance	(39.1)%	(39.1)%
Effective income tax rate	0.0%	0.0%

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**Karyopharm Therapeutics Inc.
(A Development Stage Company)**

Notes to Consolidated Financial Statements (Continued)

(in thousands, except share and per share data)

10. Income Taxes (Continued)

As of December 31, 2013 and 2012, the Company had U.S. federal net operating loss carryforwards of approximately \$45.5 million and \$27.1 million, respectively, which may be available to offset future income tax liabilities and expire at various dates through 2033. As of December 31, 2013 and 2012, the Company also had U.S. state net operating loss carryforwards of approximately \$45.9 million and \$27.1 million, respectively, which may be available to offset future income tax liabilities and expire at various dates through 2033. Included in the U.S. federal and state net operating loss carryforwards is a deduction for option exercises of \$165 and \$137 as of December 31, 2013 and 2012, respectively.

As of December 31, 2013, the Company had a Canadian net operating loss carryforward of approximately \$10.9 million, which may be available to offset future income tax liabilities and expire at various dates through 2033.

As of December 31, 2013 and 2012, the Company had federal research and development tax credit carryforwards of approximately \$2.0 million and \$665, respectively, available to reduce future tax liabilities which expire at various dates through 2033. As of December 31, 2013 and 2012, the Company had state research and development tax credit carryforwards of approximately \$1.0 million and \$206, respectively, available to reduce future tax liabilities which expire at various dates through 2028.

Under the provisions of the Internal Revenue Code, the net operating loss and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. Net operating loss and tax credit carryforwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders over a three-year period in excess of 50 percent, as defined under Sections 382 and 383 of the Internal Revenue Code, respectively, as well as similar state provisions. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. The Company has completed several financings since its inception which may have resulted in a change in control as defined by Sections 382 and 383 of the Internal Revenue Code, or could result in a change in control in the future.

The Company will recognize interest and penalties related to uncertain tax positions in income tax expense. As of December 31, 2013 and 2012, the Company had no accrued interest or penalties related to uncertain tax positions and no such amounts have been recognized in the Company's statements of operations and comprehensive loss.

For all years through December 31, 2013, the Company generated research credits but has not conducted a study to document the qualified activities. This study may result in an adjustment to the Company's research and development credit carryforwards; however, until a study is completed and any adjustment is known, no amounts are being presented as an uncertain tax position for these two years. A full valuation allowance has been provided against the Company's research and development credits and, if an adjustment is required, this adjustment would be offset by an adjustment to the deferred tax asset established for the research and development credit carryforwards and the valuation allowance.

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Karyopharm Therapeutics Inc.
(A Development Stage Company)

Notes to Consolidated Financial Statements (Continued)

(in thousands, except share and per share data)

10. Income Taxes (Continued)

The Company or one of its subsidiaries files income tax returns in the United States, and various state and foreign jurisdictions. The federal, state and foreign income tax returns are generally subject to tax examinations for the tax years ended December 31, 2010 through December 31, 2013. To the extent the Company has tax attribute carryforwards, the tax years in which the attribute was generated may still be adjusted upon examination by the Internal Revenue Service, state or foreign tax authorities to the extent utilized in a future period.

11. Subsequent Events

The Company evaluated all events and transactions that occurred after the balance sheet date through the date of this filing. During this period, the Company did not identify any material events that require accounting or disclosure in these financial statements.

12. Selected Quarterly Financial Information (Unaudited)

	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Year Ended December 31, 2013				
Contract and grant revenue	\$ 233	\$ 133	\$	\$ 21
Total operating expenses	\$ 5,844	\$ 7,003	\$ 9,321	\$ 12,169
Loss from operations	\$ (5,611)	\$ (6,870)	\$ (9,321)	\$ (12,148)
Total other income (expense)	\$	\$ 1	\$	\$ 2
Net loss	\$ (5,611)	\$ (6,869)	\$ (9,321)	\$ (12,146)
Net loss per share applicable to common stockholders, basic and diluted	\$ (2.52)	\$ (2.86)	\$ (3.66)	\$ (0.72)

	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Year Ended December 31, 2012				
Contract and grant revenue	\$ 34	\$ 533	\$ 34	\$ 33
Total operating expenses	\$ 4,017	\$ 4,567	\$ 3,669	\$ 4,271
Loss from operations	\$ (3,983)	\$ (4,034)	\$ (3,635)	\$ (4,238)
Total other income (expense)	\$ 1	\$ 1	\$	\$
Net loss	\$ (3,982)	\$ (4,033)	\$ (3,635)	\$ (4,238)
Net loss per share applicable to common stockholders, basic and diluted	\$ (2.71)	\$ (2.37)	\$ (1.97)	\$ (2.08)

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Shares

Common Stock

PROSPECTUS

BofA Merrill Lynch

Leerink Partners

JMP Securities

Wedbush PacGrow Life Sciences

Oppenheimer & Co.

, 2014

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The following table indicates the expenses to be incurred in connection with the offering described in this registration statement, other than underwriting discounts and commissions, all of which will be paid by us. All amounts are estimated except the Securities and Exchange Commission registration fee and the Financial Industry Regulatory Authority, Inc. ("FINRA") filing fee.

	Amount
Securities and Exchange Commission registration fee	\$ 14,812
FINRA filing fee	\$ 17,750
Accountants' fees and expenses	*
Legal fees and expenses	*
Transfer Agent's fees and expenses	*
Printing and engraving expenses	*
Miscellaneous	*
 Total expenses	 *

*

To be filed by amendment

Item 14. Indemnification of Directors and Officers.

Section 102 of the General Corporation Law of the State of Delaware permits a corporation to eliminate the personal liability of directors of a corporation to the corporation or its stockholders for monetary damages for a breach of fiduciary duty as a director, except where the director breached his duty of loyalty, failed to act in good faith, engaged in intentional misconduct or knowingly violated a law, authorized the payment of a dividend or approved a stock repurchase in violation of Delaware corporate law or obtained an improper personal benefit. Our certificate of incorporation provides that no director of the Registrant shall be personally liable to it or its stockholders for monetary damages for any breach of fiduciary duty as a director, notwithstanding any provision of law imposing such liability, except to the extent that the General Corporation Law of the State of Delaware prohibits the elimination or limitation of liability of directors for breaches of fiduciary duty.

Section 145 of the General Corporation Law of the State of Delaware provides that a corporation has the power to indemnify a director, officer, employee, or agent of the corporation, or a person serving at the request of the corporation for another corporation, partnership, joint venture, trust or other enterprise in related capacities against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by the person in connection with an action, suit or proceeding to which he was or is or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding by reason of such position, if such person acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the corporation, and, in any criminal action or proceeding, had no reasonable cause to believe his conduct was unlawful, except that, in the case of actions brought by or in the right of the corporation, no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or other adjudicating court determines that, despite the adjudication of liability but in view of all of the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses which the Court of Chancery or such other court shall deem proper.

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Our certificate of incorporation provides that we will indemnify each person who was or is a party or threatened to be made a party to any threatened, pending or completed action, suit or proceeding whether civil, criminal, administrative or investigative (other than an action by or in the right of us) by reason of the fact that he or she is or was, or has agreed to become, a director or officer, or is or was serving, or has agreed to serve, at our request as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (including any employee benefit plan) (all such persons being referred to as an "Indemnitee"), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees), liabilities, losses, judgments, fines (including excise taxes and penalties arising under the Employee Retirement Income Security Act of 1974), and amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding and any appeal therefrom, if such Indemnitee acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, our best interests, and, with respect to any criminal action or proceeding, he or she had no reasonable cause to believe his or her conduct was unlawful. Our certificate of incorporation provides that we will indemnify any Indemnitee who was or is a party to any threatened, pending, or completed action or suit by or in the right of us to procure a judgment in our favor by reason of the fact that the Indemnitee is or was, or has agreed to become, a director or officer, or is or was serving, or has agreed to serve, at our request as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (including any employee benefit plan), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees) and, to the extent permitted by law, amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding, and any appeal therefrom, if the Indemnitee acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, our best interests, except that no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to us, unless a court determines that, despite such adjudication but in view of all of the circumstances, he or she is entitled to indemnification of such expenses. Notwithstanding the foregoing, to the extent that any Indemnitee has been successful, on the merits or otherwise, he or she will be indemnified by us against all expenses (including attorneys' fees) actually and reasonably incurred in connection therewith. Expenses must be advanced to an Indemnitee under certain circumstances.

We have entered into indemnification agreements with each of our directors. These indemnification agreements may require us, among other things, to indemnify our directors for some expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by a director in any action or proceeding arising out of his or her service as one of our directors, or any of our subsidiaries or any other company or enterprise to which the person provides services at our request.

We maintain a liability insurance policy that covers certain liabilities of directors and officers of our corporation arising out of claims based on acts or omissions in their capacities as directors or officers.

In any underwriting agreement we enter into in connection with the sale of common stock being registered hereby, the underwriters will agree to indemnify, under certain conditions, us, our directors, our officers and persons who control us within the meaning of the Securities Act of 1933, as amended (the "Securities Act"), against certain liabilities.

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Item 15. Recent Sales of Unregistered Securities.

Set forth below is information regarding shares of capital stock issued by us within the past three years. Also included is the consideration received by us for such shares and information relating to the section of the Securities Act, or rule of the Securities and Exchange Commission, under which exemption from registration was claimed.

(a)

Issuances of Preferred Stock

In February 2012, we entered into a stock purchase agreement for the purpose of issuing and selling up to an aggregate of 1,538,461 shares of our series A-4 preferred stock, at a purchase price per share of \$1.30, for an aggregate purchase price of \$1,999,999. We issued these shares in August 2013.

In October 2011, we entered into a stock purchase agreement for the purpose of issuing and selling up to an aggregate of (i) 7,000,000 shares of our series A-2 preferred stock and (ii) 3,000,000 shares of our series A-3 preferred stock. Between October 2011 and February 2013, we became obligated to issue 6,100,000 shares of our series A-2 preferred stock at a purchase price per share of \$1.15, for an aggregate purchase price of \$7,015,000, and 1,764,706 shares of our series A-3 preferred stock at a purchase price per share of \$1.70, for an aggregate purchase price of \$3,000,000. We issued these shares in August 2013.

In July 2013, we issued and sold an aggregate of 8,636,362 shares of our series B-1 preferred stock at a price per share of \$2.20 for an aggregate purchase price of \$18,999,996.

Between April and September 2013, we issued and sold an aggregate of 24,100,000 shares of our series B preferred stock at a price per share of \$2.00 for an aggregate purchase price of \$48,200,000.

Between October 2010 and January 2013, we issued and sold an aggregate of 20,937,500 shares of our series A preferred stock, at a purchase price per share of \$1.00, for an aggregate purchase price of \$20,937,500.

No underwriters were involved in the foregoing sales of securities. The securities described in this section (a) of Item 15 were issued to third parties pursuant to Regulation D promulgated under the Securities Act or pursuant to Regulation S promulgated under the Securities Act, in each case related to transactions by an issuer not involving any public offering. All purchasers of shares of preferred stock described above represented to us in connection with their purchase that they were accredited investors, and were acquiring the shares for their own account for investment purposes only and not with a view to, or for sale in connection with, any distribution thereof and that they could bear the risks of the investment. The purchasers received written disclosures that the securities had not been registered under the Securities Act and that any resale must be made pursuant to a registration statement or an available exemption from such registration.

(b)

Issuances of Common Stock

In July 2013, we issued an aggregate of 12,121 shares of our common stock to the holders of our special participation stock, in connection with the election of the holders of a majority of such shares of special participation stock to convert all outstanding shares of special participation stock into common stock.

In December 2011, we issued an aggregate of 45,454 shares of our common stock to two of our directors, each of whom was also providing consulting services to us at that time, at a purchase price per share of \$0.26, for an aggregate purchase price of \$12,000.

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In March 2011, we issued an aggregate of 162,684 shares of our common stock to a service provider in consideration for services provided to us under a master services agreement with such service provider.

The common stock described in this section (b) of Item 15 was issued pursuant to (i) with respect to the shares issued in July 2013, the exemption from the registration requirements of the Securities Act provided by Section 3(a)(9) of the Securities Act, (ii) with respect to the shares issued in December 2011, qualified written compensatory plans or arrangements with our employees, directors, officers, consultants and advisors, in reliance on the exemption from registration provided by Rule 701 promulgated under the Securities Act, or (iii) with respect to the shares issued in March 2011, in reliance on the exemption from registration provided by Section 4(2) under the Securities Act, relative to transactions by an issuer not involving any public offering. All recipients either received adequate information about us or had access, through employment or other relationships, to such information.

(c)

Stock Option Grants

Since January 1, 2011 and through December 31, 2013, we have issued to certain employees, directors and consultants options to purchase an aggregate of 2,804,677 shares of common stock, of which options issued between January 1, 2011 and December 31, 2013, as of December 31, 2013, options to purchase 452,107 shares of common stock had been exercised, options to purchase 113,836 shares had been forfeited and options to purchase 2,238,735 shares of common stock remained outstanding at a weighted-average exercise price of \$8.44 per share.

The issuance of stock options and the common stock issuable upon the exercise of such options as described in this section (c) of Item 15 were issued pursuant to written compensatory plans or arrangements with our employees, directors and consultants, in reliance on the exemption from the registration requirements of the Securities Act provided by Rule 701 promulgated under the Securities Act, or pursuant to Section 4(2) under the Securities Act. All recipients either received adequate information about us or had access, through employment or other relationships, to such information.

Item 16. Exhibits and Financial Statement Schedules.

(a)

Exhibits.

The exhibits to this registration statement are listed in the Exhibit Index attached hereto and incorporated by reference herein.

Item 17. Undertakings.

The undersigned registrant hereby undertakes to provide to the underwriters, at the closing specified in the underwriting agreement, certificates in such denominations and registered in such names as required by the underwriters to permit prompt delivery to each purchaser.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

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The undersigned hereby undertakes that:

- (1) For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.
- (2) For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

Table of Contents**SIGNATURES AND POWER OF ATTORNEY**

We, the undersigned officers and directors of Karyopharm Therapeutics Inc., hereby severally constitute and appoint Michael Kauffman, M.D., Ph.D. and Paul Brannelly, and each of them singly (with full power to each of them to act alone), our true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution in each of them for him and in his name, place and stead, and in any and all capacities, to sign any and all amendments (including post-effective amendments) to this registration statement (or any other registration statement for the same offering that is to be effective upon filing pursuant to Rule 462(b) under the Securities Act of 1933), and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite or necessary to be done in and about the premises, as full to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents or any of them, or their or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this Registration Statement has been signed by the following persons in the capacities held on the dates indicated.

Signature	Title	Date
<u>/s/ MICHAEL G. KAUFFMAN</u> Michael G. Kauffman, M.D., Ph.D.	Chief Executive Officer and Director (principal executive officer)	March 24, 2014
<u>/s/ PAUL BRANNELLY</u> Paul Brannelly	Senior Vice President, Finance and Administration, and Treasurer (principal financial and accounting officer)	March 24, 2014
<u>/s/ GAREN G. BOHLIN</u> Garen G. Bohlin	Director	March 24, 2014
<u>/s/ BARRY E. GREENE</u> Barry E. Greene	Director	March 24, 2014
<u>/s/ DEEPA R. PAKIANATHAN</u> Deepa R. Pakianathan, Ph.D.	Director	March 24, 2014
<u>/s/ MANSOOR RAZA MIRZA</u> Mansoor Raza Mirza, M.D.	Director	March 24, 2014
<u>/s/ KENNETH E. WEG</u> Kenneth E. Weg	Director	March 24, 2014

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Exhibit Number	Description of Exhibit
	<i>Underwriting Agreement</i>
1.1*	Underwriting Agreement
	<i>Articles of Incorporation and Bylaws</i>
3.1	Restated Certificate of Incorporation of the Registrant(1)
3.2	Amended and Restated By-Laws of the Registrant(1)
	<i>Instruments Defining the Rights of Security Holders, Including Indentures</i>
4.1	Specimen Stock Certificate evidencing the shares of common stock(2)
4.2	Third Amended and Restated Investors' Rights Agreement dated as of July 26, 2013(3)
	<i>Opinion re Legality</i>
5.1*	Opinion of Wilmer Cutler Pickering Hale and Dorr LLP
	<i>Material Contracts Management Contracts and Compensatory Plans</i>
10.1	2010 Stock Incentive Plan(3)
10.2	Forms of Non-Qualified Stock Option Agreement under 2010 Stock Incentive Plan(3)
10.3	2013 Stock Incentive Plan(2)
10.4	Form of Incentive Stock Option Agreement under 2013 Stock Incentive Plan(2)
10.5	Form of Nonstatutory Stock Option Agreement under 2013 Stock Incentive Plan(2)
10.6	2013 Employee Stock Purchase Plan(2)
10.7	Employment Agreement dated December 6, 2010 between the Registrant and Michael Kauffman, M.D., Ph.D.(2)
10.8	Employment Agreement dated October 19, 2010, as amended on December 6, 2010, between the Registrant and Sharon Shacham, Ph.D., M.B.A.(2)
10.9	Employment Agreement dated May 29, 2013 between the Registrant and Paul Brannelly(2)
10.10	Consulting Agreement, dated as of October 28, 2010, between the Registrant and Alan T. Barber(3)
10.11	Consulting Agreement, dated as of September 1, 2012, between the Registrant and Mirza Consulting(3)
10.12	Form of Indemnification Agreement between the Registrant and each of its Directors(3)
10.13	Offer Letter from the Registrant to Christopher Primiano dated March 3, 2014(4)
	<i>Material Contracts Leases</i>
10.14	Lease, dated as of December 10, 2010, as amended on January 10, 2012 and July 29, 2013, between the Registrant and Nivek Investments I, LLC(3)

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Exhibit Number	Description of Exhibit
	<i>Material Contracts Research Agreements</i>
10.15	Research Agreement, dated as of July 18, 2011, between the Registrant and the Multiple Myeloma Research Foundation, Inc.(3)
	<i>Additional Exhibits</i>
21.1	Subsidiaries of the Registrant(4)
23.1	Consent of McGladrey LLP
23.2*	Consent of Wilmer Cutler Pickering Hale and Dorr LLP (included in Exhibit 5.1)
24.1	Power of Attorney (included on signature page)
101.INS XBRL**	Instance Document
101.SCH XBRL**	Schema Document
101.CAL XBRL**	Calculation Linkbase Document
101.LAB XBRL**	Labels Linkbase Document
101.PRE XBRL**	Presentation Linkbase Document
101.DEF XBRL**	Definition Linkbase Document

*

To be filed by amendment.

Confidential treatment has been granted as to portions of the exhibit.

**

Pursuant to Rule 406T of Regulation S-T, these interactive data files are furnished and not filed or part of a registration statement or prospectus for purposes of Sections 11 or 12 of the Securities Act of 1933 or Section 18 of the Securities Exchange Act of 1934 and otherwise are not subject to liability under these sections.

(1)

Incorporated by reference to the Registrant's Current Report on Form 8-K (File No. 001-36167) filed with the Securities and Exchange Commission on November 18, 2013.

(2)

Incorporated by reference to the Registrant's Amendment No. 1 to Registration Statement on Form S-1 (File No. 333-191584) filed with the Securities and Exchange Commission on October 28, 2013.

(3)

Incorporated by reference to the Registrant's Registration Statement on Form S-1 (File No. 333-191584) filed with the Securities and Exchange Commission on October 4, 2013.

(4)

Incorporated by reference to the Registrant's Annual Report on Form 10-K (File No. 001-36167) filed with the Securities and Exchange Commission on March 21, 2014.