EXELIXIS INC
Form 424B5
August 06, 2012
Table of Contents

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Registration No. 333-182018

The information in this preliminary prospectus supplement is not complete and may be changed. This preliminary prospectus supplement is not an offer to sell nor does it seek an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to Completion. Dated August 6, 2012.

Prospectus Supplement to Prospectus dated June 8, 2012.

20,000,000 Shares

Common Stock

Exelixis, Inc. is offering 20,000,000 shares to be sold in the offering.

The common stock is quoted on The NASDAQ Global Select Market under the symbol EXEL. The last reported sale price of the common stock on August 3, 2012, was $5.58 per share.

Concurrently with this offering of common stock, we are offering $225.0 million aggregate principal amount of convertible senior subordinated notes due 2019 (the notes) (or a total of $258.8 million aggregate principal amount if the underwriters for the concurrent notes offering exercise in full their option to purchase additional notes) pursuant to a separate prospectus supplement.

See Risk Factors beginning on page S-10 of this prospectus supplement to read about factors you should consider before buying shares of the common stock.

Neither the Securities and Exchange Commission nor any other regulatory body has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

	Per Share	Total
Initial price to public	$	$
Underwriting discount	$	$
Proceeds, before expenses, to Exelixis	$	$

To the extent that the underwriters sell more than 20,000,000 shares of common stock, the underwriters have the option to purchase up to an additional 3,000,000 shares from Exelixis at the initial price to public less the underwriting discount.

The underwriters expect to deliver the shares against payment in New York, New York on August , 2012.

Joint Book-Running Managers

Goldman, Sachs & Co. **Cowen and Company**

Co-Managers

Piper Jaffray **Stifel Nicolaus Weisel** **William Blair**

Prospectus Supplement dated August , 2012.

Table of Contents

TABLE OF CONTENTS

Prospectus Supplement

Prospectus

Table of Contents

ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of the common stock we are offering. The second part, the accompanying prospectus dated June 8, 2012, gives more general information about our common stock. You should read this prospectus supplement and the accompanying prospectus, including the information incorporated by reference and any free writing prospectuses we have authorized for use in connection with this offering, in their entirety before making an investment decision.

You should rely only on the information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus, along with the information contained in any free writing prospectuses we have authorized for use in connection with this offering. If the description of the offering varies between this prospectus supplement and the accompanying prospectus, you should rely on the information in this prospectus supplement. We have not authorized anyone to provide you with different or additional information. Under no circumstances should the delivery to you of this prospectus supplement and the accompanying prospectus or any sale made pursuant to this prospectus supplement create any implication that the information contained in this prospectus supplement or the accompanying prospectus is correct as of any time after the respective dates of such information.

Unless the context requires otherwise, the words Exelixis, we, the company, us and our refer to Exelixis, Inc. and its subsidiaries, and the ter you refers to a prospective investor.

This prospectus supplement and the accompanying prospectus, including the information incorporated by reference into this prospectus supplement and the accompanying prospectus, include trademarks, service marks and trade names owned by us or others. Exelixis, Inc., the Exelixis, Inc. logo and all other Exelixis product and service names are trademarks of Exelixis, Inc. in the United States and in other selected countries. All other trademarks, service marks and trade names included or incorporated by reference in this prospectus supplement and the accompanying prospectus are the property of their respective owners.

Table of Contents

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information appearing elsewhere or incorporated by reference in this prospectus supplement and accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering and may not contain all of the information that is important to you. This prospectus supplement and the accompanying prospectus include information about the shares we are offering as well as information regarding our business and financial data. You should read this prospectus supplement and the accompanying prospectus, including the information incorporated by reference and any free writing prospectuses we have authorized for use in connection with this offering, in their entirety. Investors should carefully consider the information set forth under Risk Factors in this prospectus supplement.

Exelixis, Inc.

We are a biotechnology company committed to developing small molecule therapies for the treatment of cancer. We are focusing our proprietary resources and development efforts exclusively on cabozantinib, formerly known as XL184, our most advanced product candidate, in order to maximize the therapeutic and commercial potential of this compound. We believe cabozantinib has the potential to be a high-quality, broadly-active, differentiated pharmaceutical product that can make a meaningful difference in the lives of patients. We have also established a portfolio of other novel compounds that we believe have the potential to address serious unmet medical needs, many of which are being advanced by partners as part of collaborations.

Cabozantinib

Cabozantinib inhibits MET, VEGFR2 and RET, proteins that are key drivers of tumor growth, vascularization, and/or metastasis. Cabozantinib has shown novel and differentiated activity in multiple cancer indications. The current clinical program for cabozantinib is focused on the treatment of metastatic castration-resistant prostate cancer, or CRPC, and medullary thyroid cancer but also includes the evaluation of other tumor types.

Exelixis has implemented a strategy to investigate cabozantinib in a comprehensive development program for CRPC to potentially generate a product that could effectively compete in the CRPC marketplace. Two phase 3 pivotal trials, COMET-1 (CabOzantinib MET Inhibition CRPC Efficacy Trial-1, formerly known as XL184-307) and COMET-2 (CabOzantinib MET Inhibition CRPC Efficacy Trial-2, formerly known as XL184-306), were designed to provide an opportunity to commercially differentiate cabozantinib as an oncology agent with a potentially beneficial impact on overall survival, pain palliation and narcotic usage. We initiated the COMET-2 trial with a pain palliation endpoint in December 2011 and the COMET-1 trial with an overall survival endpoint in May 2012.

In May 2012, we completed the submission of our rolling new drug application, or NDA, with the United States Food and Drug Administration, or FDA, for cabozantinib as a treatment for medullary thyroid cancer. On July 30, 2012, we announced that the FDA has accepted our NDA for filing and granted a Priority Review designation with a stated action date of November 29, 2012. The NDA submission was based on the data from our phase 3 clinical trial of cabozantinib as a potential treatment for medullary thyroid cancer, known as the EXAM trial (Efficacy of XL184 (Cabozantinib) in Advanced Medullary Thyroid Cancer), with progression-free survival, or PFS, as the trial s primary endpoint. The EXAM trial has been conducted under a special protocol assessment, or SPA, with the FDA, which allows for full approval on the basis of PFS if the data are supportive. We announced in October 2011 that the primary endpoint of the EXAM trial had been met. Data from the EXAM trial was

reported at the American Society of Clinical Oncology Annual Meeting, or ASCO, in June 2012. Assuming approval of our NDA by the FDA, we currently anticipate a potential commercial launch of cabozantinib for the treatment of medullary thyroid cancer in late 2012 or early 2013.

We expect to expand the cabozantinib development program to other solid tumor indications, based on encouraging interim data that have emerged from the randomized discontinuation trial, or RDT, investigating cabozantinib in 9 distinct tumor types, as well as other clinical trials. Objective tumor responses have been observed in patients treated with cabozantinib in 12 of 13 individual tumor types investigated to date, reflecting the broad potential clinical activity and commercial opportunity of this new product candidate. Interim data suggest that cabozantinib has shown novel activity against bone and soft tissue lesions in patients with CRPC. We have also observed resolution of metastatic bone lesions on bone scan in patients with metastatic breast cancer, renal cell carcinoma, thyroid cancer, and melanoma.

Interim data from the CRPC cohort of the RDT reported at ASCO in June 2011 demonstrated that in addition to improvement of bone lesions on bone scan observed in the majority (75%) of patients, 67% of patients with bone metastases and bone pain at baseline also experienced alleviation of pain. This observation has been corroborated in a non-randomized expansion cohort, or NRE, of CRPC patients in the RDT, which collected prospectively defined patient reported outcomes on pain and narcotic use. Interim data reported at ASCO in June 2012 demonstrated that 64% of CRPC patients with moderate to severe pain in the NRE experienced durable pain reduction greater than or equal to 30%. The median best pain reduction was 46%. In addition, these interim data indicated that 56% of CRPC patients in the NRE with moderate to severe bone pain and on narcotics at baseline were able to reduce or discontinue narcotic medication. These interim data also indicated that 92% of evaluable CRPC patients in the NRE experienced a reduction greater than or equal to 30% in their circulating tumor cell, or CTC, count.

Lower starting doses of cabozantinib are being evaluated through a dose-ranging study in CRPC patients conducted through an investigator-sponsored trial, or IST. Interim data from this dose-ranging IST reported at ASCO in June 2012 demonstrated that a daily dose of 40 mg resulted in a rate of bone scan responses similar to that of a 100 mg daily dose used in the RDT, and was associated with improved tolerability compared with the higher dose. The interim data from the IST reported at ASCO in June 2012 also indicated that 92% of evaluable CRPC patients in the 40 mg dose cohort of the IST experienced a reduction greater than or equal to 30% in their CTC count. Interim data from a cohort of CRPC patients in the NRE treated at a daily dose of 40 mg has demonstrated pain palliation responses consistent with observations at the 100 mg daily dose.

We believe that cabozantinib s clinical profile is compelling and will allow commercial differentiation, assuming regulatory approval. Accordingly, it is a priority for us to generate additional data from the RDT as well as other ongoing exploratory clinical trials for cabozantinib in a broad range of tumor types, including ovarian cancer, melanoma, breast cancer, non-small cell lung cancer, hepatocellular cancer, renal cell carcinoma, and differentiated thyroid cancer, to support further prioritization of our clinical and commercial options. We have launched two initiatives to expand the cabozantinib development program beyond our internal development efforts: our IST program and our Cooperative Research and Development Agreement, or CRADA, with the National Cancer Institute s Cancer Therapy Evaluation Program, or NCI-CTEP.

We launched the IST program in 2011, and it has already provided important interim data through the dose-ranging study in CRPC patients described above. These data were important for dose selection in the COMET pivotal trial program, and we believe they will guide dose selection for a

Table of Contents

potential future trial to evaluate the ability of cabozantinib to prevent bone metastases in men with prostate cancer. Other recently initiated ISTs include:

- Phase 2 clinical trial of cabozantinib in women with hormone receptor-positive metastatic breast cancer and bone metastases.
- Phase 1b clinical trial evaluating cabozantinib in combination with abiraterone in CRPC patients.
- Phase 2 clinical trial of cabozantinib in chemotherapy naïve CRPC patients with bone metastases.
- Phase 1b clinical trial evaluating cabozantinib in combination with androgen ablation in patients with androgen-dependent metastatic prostate cancer.
- Phase 2 clinical trial using magnetic resonance imaging to measure the effect of cabozantinib on bone metastases in patients with CRPC.
- Phase 1 clinical trial of cabozantinib in patients with relapsed or refractory multiple myeloma with bone disease.
- Phase 2 clinical trial evaluating cabozantinib in patients with advanced pancreatic neuroendocrine and carcinoid tumors.
- Phase 2 clinical trial of cabozantinib in patients with KIF5B/RET-positive advanced non-small cell lung cancer.
- Phase 2 clinical trial evaluating cabozantinib in patients with advanced solid malignancies and bone metastases.

We plan to further expand the IST program with new trials this year.

We entered into our CRADA with NCI-CTEP in November 2011, under which thirteen proposed clinical trials have been approved to date, as follows:

- Phase 2 clinical trials in disease settings where there is substantial unmet medical need and in which cabozantinib has previously demonstrated clinical activity, consisting of randomized phase 2 clinical trials in first line renal cell carcinoma, second line hepatocellular carcinoma, platinum-resistant or refractory ovarian cancer, ocular melanoma, second line non-small cell lung cancer, and second line/third line non-small cell lung cancer. We believe that data from these phase 2 clinical trials will help prioritize future phase 3 pivotal trials of cabozantinib.
- Additional phase 2 clinical trials to explore cabozantinib s potential utility in other tumor types, consisting of trials in endometrial cancer, bladder cancer, sarcoma and second line differentiated thyroid cancer. Positive results in these indications could lead to further study in randomized phase 2 or phase 3 clinical trials.

Additional phase 1 clinical trials, consisting of a trial evaluating cabozantinib in combination with docetaxel in CRPC patients, a trial exploring the utility of combining cabozantinib with vemurafenib, a BRAF inhibitor, in patients with BRAF-mutated melanoma, and a trial to evaluate the safety and phamacokinetics of cabozantinib in pediatric malignancies.

Commencement of each of the proposed trials approved under the CRADA is subject to protocol development and satisfaction of certain other conditions. The proposed trials approved under the CRADA will be conducted under an investigational new drug application held by NCI-CTEP. We believe our CRADA reflects a major commitment by NCI-CTEP to support the broad exploration of

Table of Contents

cabozantinib s potential in a wide variety of cancers that have substantial unmet medical needs. Since NCI-CTEP provides funding for as many as 20 active clinical trials each year for a five year period, we believe the agreement will enable us to broadly expand the cabozantinib development program in a cost-efficient manner.

Collaborations

We have established collaborations with leading pharmaceutical and biotechnology companies, including Bristol-Myers Squibb Company, or Bristol-Myers Squibb, Sanofi, Genentech, Inc. (a wholly- owned member of the Roche Group), GlaxoSmithKline, Merck (known as MSD outside of the United States and Canada) and Daiichi Sankyo Company Limited, or Daiichi Sankyo, for various compounds and programs in our portfolio. Pursuant to these collaborations, we have out-licensed compounds or programs to a partner for further development and commercialization, generally have no further unfunded cost obligations related to such compounds or programs and may be entitled to receive research funding, milestones and royalties or a share of profits from commercialization. Several of the out-licensed compounds are in multiple phase 2 studies and could potentially be of significant value to us if their development progresses successfully. With respect to our partnered compounds, we are eligible to receive potential milestone payments under our collaborations totaling approximately $3.1 billion in the aggregate on a non-risk adjusted basis, of which 10% are related to clinical development milestones, 44% are related to regulatory milestones and 46% are related to commercial milestones.

Corporate Information

We were incorporated in Delaware in November 1994 as Exelixis Pharmaceuticals, Inc. and we changed our name to Exelixis, Inc. in February 2000. Our principal executive offices are located at 210 East Grand Ave., South San Francisco, California 94080. Our telephone number is (650) 837-7000 and our website is http://www.exelixis.com. We have not incorporated by reference into this prospectus supplement or the accompanying prospectus the information on our website, and you should not consider it to be a part of this prospectus supplement. Our website address is included in this prospectus supplement as an inactive textual reference only.

Table of Contents

The Offering

Common stock offered by Exelixis	20,000,000 shares
Underwriters option to purchase additional shares	3,000,000 shares
Common stock to be outstanding after the offering	168,794,245 shares
Use of proceeds	We currently expect to use the net proceeds from this offering and the offering of our convertible senior subordinated notes (referenced below) for general corporate purposes, including for clinical trials, research and development, capital expenditures and working capital. In addition, we have agreed to place approximately $ million (or approximately $ million if the underwriters exercise their option to purchase additional notes in full) of the proceeds of the concurrent notes offering in an escrow account with the trustee under the indenture pursuant to which the notes are issued. See Use of Proceeds in this prospectus supplement.
Concurrent notes offering	Concurrently with this offering of common stock, we are offering $225.0 million aggregate principal amount of notes (or a total of $258.8 million aggregate principal amount if the underwriters for the concurrent notes offering exercise in full their option to purchase additional notes) pursuant to a separate prospectus supplement. See Concurrent Convertible Notes Offering in this prospectus supplement. We expect to raise approximately $217.9 million in net proceeds from the concurrent notes offering (approximately $250.6 million if the underwriters for the concurrent notes offering exercise in full their option to purchase additional notes), after deducting the estimated underwriting discounts and estimated offering expenses payable by us. See Use of Proceeds in this prospectus supplement. This prospectus supplement shall not be deemed an offer to sell or a solicitation of an offer to buy any of the notes offered in the concurrent notes offering. The common stock offering is not contingent upon the concurrent notes offering, and the concurrent notes offering is not contingent upon this common stock offering. We cannot assure you that either or both of the offerings will be completed.

Table of Contents

	Unless we specifically state otherwise, the information in this prospectus supplement assumes the completion of the concurrent notes offering, and that the underwriters for the concurrent notes offering do not exercise their option to purchase additional notes in that offering.
Risk factors	See Risk Factors beginning on page S-10 for a discussion of factors you should consider before buying shares of our common stock.
NASDAQ Global Select Market Symbol	EXEL

The number of shares of common stock to be outstanding after the offering is based on the number of shares outstanding as of June 30, 2012. As of that date, we had 148,794,245 shares of common stock outstanding, excluding:

- 16,345,993 shares of common stock underlying options outstanding as of June 30, 2012, at a weighted average exercise price of $7.06 per share;
- 1,441,215 shares of common stock underlying warrants outstanding as of June 30, 2012, at a weighted average exercise price of $6.99 per share;
- 907,697 shares reserved for future issuance pursuant to unvested restricted stock units as of June 30, 2012;
- 10,508,305 shares available for future grant under our 2011 Equity Incentive Plan, 2,481,973 shares available for future grant under our 2000 Employee Stock Purchase Plan, 987,656 shares available for future grant under our 2000 Non-Employee Directors Stock Option Plan, and 568,062 shares available for future grant under our 401(k) Retirement Plan, all as of June 30, 2012; and
- shares of common stock reserved for issuance upon conversion of the convertible notes being offered by us in connection with our concurrent notes offering.

Unless we specifically state otherwise, the information in this prospectus supplement assumes that the underwriters in this offering and in the concurrent notes offering do not exercise their option to purchase up to 3,000,000 additional shares of our common stock in this offering or $33.8 million aggregate principal amount of the notes in the concurrent notes offering, respectively, within 30 days after the date of this prospectus supplement.

Table of Contents

Summary Consolidated Financial Data

We derived the information presented below as of December 31, 2011, and for each of the three years ended December 31, 2009, 2010 and 2011, from our audited consolidated financial statements. We derived the information presented below as of June 30, 2012, and for each of the six months ended June 30, 2011 and 2012, from our unaudited condensed consolidated financial statements. In the opinion of management, all adjustments, consisting of only normal recurring adjustments, necessary for a fair presentation of the unaudited financial data as of June 30, 2012, and for each of the six months ended June 30, 2011 and 2012, have been reflected therein. Operating results for the six months ended June 30, 2012, are not necessarily indicative of the results that may be expected for the full year. The following information should be read in conjunction with our consolidated financial statements and related notes incorporated by reference in this prospectus supplement and the accompanying prospectus from our Annual Report on Form 10-K for the fiscal year ended December 31, 2011, and our Quarterly Report on Form 10-Q for the fiscal quarter ended June 30, 2012.

The as adjusted balance sheet data as of June 30, 2012, reflects receipt of the estimated net proceeds of $105.6 million from the sale of the common stock in this offering (assuming no exercise of the underwriters option to purchase additional shares) at an assumed public offering price of $5.58 per share, the closing price of our common stock on August 3, 2012, and the estimated net proceeds of $217.9 million from the issuance of $225.0 million principal amount of the notes (assuming no exercise of the underwriters option to purchase additional notes) in our concurrent notes offering, in each case, after deducting the estimated underwriting discounts and estimated offering expenses payable by us as described under Use of Proceeds.

For more details on how you can obtain our SEC reports and other information, you should read the section of the accompanying prospectus entitled Where You Can Find More Information.

	Year Ended December 31,			Six Months Ended June 30,	
	2009	2010	2011	2011	2012
				(unaudited)	
	(in thousands, except per share data)				
Consolidated Statement of Operations Data					
Total revenues	$ 151,759	$ 185,045	$ 289,636	$ 68,056	$ 26,323
Total operating expenses	$ 273,666	$ 276,442	$ 200,101	$ 109,794	$ 81,342
Consolidated net (loss) income	$ (139,557)	$ (92,330)	$ 75,697	$ (48,464)	$ (62,638)
Loss attributed to noncontrolling interest	$ 4,337	$	$	$	$
Net (loss) income attributable to Exelixis, Inc.	$ (135,220)	$ (92,330)	$ 75,697	$ (48,464)	$ (62,638)
Net (loss) income per share, basic attributable to Exelixis, Inc.	$ (1.26)	$ (0.85)	$ 0.60	$ (0.40)	$ (0.43)
Net (loss) income per share, diluted attributable to Exelixis, Inc.	$ (1.26)	$ (0.85)	$ 0.58	$ (0.40)	$ (0.43)
Shares used in computing basic net (loss) income per share	107,073	108,522	126,018	120,768	145,297
Shares used in computing diluted net (loss) income per share	107,073	108,522	130,479	120,768	145,297

	As of June 30, 2012	
	Actual	As Adjusted(2)
	(unaudited)	
	(in thousands)	
Consolidated Balance Sheet Data		
Cash and cash equivalents, marketable securities, restricted cash and investments and long-term investments(1)(3)	$ 294,786	$ 616,756
Working capital(1)(3)	$ 123,676	$
Total assets(1)(3)	$ 374,488	$ 705,108
% Convertible senior subordinated notes due 2019(2)	$	$
Debt obligations under the loan and security agreement with SVB	$ 86,836	$ 86,836
Debt obligations under the Deerfield Notes	$ 95,862	$ 95,862
Additional paid-in-capital(2)	$ 1,267,890	$
Total stockholders equity(2)	$ 99,049	$

Table of Contents

(1) Each $1.00 increase or decrease in the assumed offering price per share would increase or decrease the as adjusted amount shown above for each of cash and cash equivalents, marketable securities, restricted cash and investments and long-term investments, working capital and total assets by approximately $19.0 million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus supplement, remains the same and after deducting the estimated underwriting discounts and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. An increase or decrease of 500,000 shares in the number of shares offered by us at the assumed offering price would increase or decrease the as adjusted amount above for each of cash and cash equivalents, marketable securities, restricted cash and investments and long-term investments, working capital and total assets by approximately $2.7 million, after deducting the estimated underwriting discounts and estimated offering expenses payable by us. The as adjusted amounts shown above do not reflect the placement of amounts in the interest escrow, as described under Use of Proceeds. Such amounts will be classified as restricted cash.

(2) Amounts shown reflect the application of Financial Accounting Standards Board Staff Position No. APB 14-1, as codified by Accounting Standards Codification 470-20, or ASC 470-20, which requires issuers to separately account for the liability and equity components of convertible debt instruments that may be settled entirely or partially in cash. The determination of the fair values of the debt and equity components has been estimated but is subject to change based upon the completion of our analysis of non-convertible debt interest rates. In accordance with ASC 470-20, we estimate that approximately $ million of the aggregate principal amount of the notes offered in our concurrent notes offering will be recognized as the equity component. The determination of the fair values of the debt and equity components has been estimated but is subject to change based upon the completion of our analysis of non-convertible debt interest rates.

(3) The as adjusted amounts reflect the cash payment of a $1.5 million consent fee to entities affiliated with Deerfield Management Company L.P., or Deerfield.

Our Fiscal Year

We have adopted a 52- or 53-week fiscal year that ends on the Friday closest to December 31st. Fiscal year 2009, a 52-week year, ended on January 1, 2010, fiscal year 2010, a 52-week year, ended on December 31, 2010, fiscal year 2011, a 52-week year, ended on December 30, 2011, and fiscal year 2012, a 52-week year, will end on December 28, 2012. For convenience, references in this prospectus supplement as of and for the fiscal years ended January 1, 2010, December 31, 2010, and December 30, 2011, and as of and for the fiscal quarters ended July 1, 2011, and June 29, 2012, are indicated on a calendar year basis as ended December 31, 2009, 2010 and 2011, and June 30, 2011 and 2012, respectively.

Table of Contents

RISK FACTORS

Investing in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, you should consider carefully the risk factors described below and in any free writing prospectus that we have authorized for use in connection with this offering. If any of these risks actually occur, it may materially harm our business, financial condition, operating results or cash flow. As a result, the market price of our common stock could decline, and you could lose all or part of your investment. Additional risks and uncertainties that are not yet identified or that we think are immaterial may also materially harm our business, operating results and financial condition and could result in a complete loss of your investment.

Risks Related to Our Need for Additional Financing and Our Financial Results

If additional capital is not available to us, we would be forced to delay, reduce or eliminate our product development programs or commercialization efforts and we may breach our financial covenants.

We will need to raise additional capital to:

- fund our operations and clinical trials;
- continue our research and development efforts; and
- commercialize our product candidates, if any such candidates receive regulatory approval for commercial sale.

As of June 30, 2012, we had $294.8 million in cash and cash equivalents, marketable securities and long-term investments, which included restricted cash and investments of $4.1 million and approximately $83.7 million of cash and cash equivalents and marketable securities that we are required to maintain on deposit with Silicon Valley Bank, or SVB, or one of its affiliates pursuant to covenants in our loan and security agreement with SVB. We anticipate that our current cash and cash equivalents, marketable securities, long-term investments and funding that we expect to receive from existing collaborators, together with the anticipated proceeds from this offering and our concurrent notes offering, will enable us to maintain our operations for a period of at least 12 months following the end of the second quarter of 2012. However, our future capital requirements will be substantial, and we will need to raise additional capital in the future. Our capital requirements will depend on many factors, and we may need to use available capital resources and raise additional capital significantly earlier than we currently anticipate. These factors include:

- the progress and scope of the cabozantinib development program: We are focusing our proprietary resources and development efforts on cabozantinib, our most advanced product candidate, which is being studied in a variety of tumor types, with the goal of rapidly commercializing the compound. Cabozantinib is being evaluated in a broad development program encompassing multiple cancer indications. The current clinical program for cabozantinib is focused on the treatment of CRPC and medullary thyroid cancer and will be expanded to other solid tumor indications, based on encouraging interim data that have emerged from the RDT investigating cabozantinib in nine distinct tumor types and other clinical trials. In October 2011, we announced that our EXAM phase 3 clinical trial of cabozantinib in medullary thyroid cancer met its primary endpoint and on July 30, 2012, we announced that the FDA has accepted our NDA, based on data from our EXAM trial, for filing and granted a Priority Review designation with a stated action date of November 29, 2012. Assuming approval of our NDA by the FDA, we currently anticipate a potential commercial launch of cabozantinib for the treatment of medullary thyroid cancer in late 2012 or early 2013. As part of our comprehensive development plan for cabozantinib in CRPC, in December 2011, we initiated our first phase 3 pivotal trial of cabozantinib in patients with CRPC using an endpoint of pain reduction (COMET-2) and in May 2012 we initiated a second phase 3 pivotal trial in patients with CRPC with

Table of Contents

an overall survival endpoint (COMET-1). We are also planning other potential pivotal trials in prostate cancer. Our development and commercialization plans for cabozantinib are dependent on the extent of our available financial resources. There can be no assurance that we will have sufficient financial resources independently or through other arrangements to fund the trials that are currently planned or in process, to fund other clinical trials that we may desire to initiate in the future or to fund commercialization efforts. If adequate funds are not available, we may be required to delay, discontinue or elect not to pursue one or more trials or commercialization efforts for cabozantinib;

repayment of our secured convertible notes we previously issued to Deerfield, which we refer to as the Deerfield Notes: On June 2, 2010, we entered into a note purchase agreement with Deerfield, pursuant to which, on July 1, 2010, we sold to Deerfield an aggregate of $124.0 million initial principal amount of the Deerfield Notes, due June 2015, for an aggregate purchase price of $80.0 million, less closing fees and expenses. The outstanding principal amount of the Deerfield Notes bears interest in the annual amount of $6.0 million, payable quarterly in arrears. We will be required to make mandatory prepayments on the Deerfield Notes on an annual basis in 2013, 2014 and 2015 equal to 15% of specified payments from our collaborative arrangements received during the prior fiscal year, subject to a maximum annual prepayment amount of $27.5 million and, for payments due in January 2013 and 2014, a minimum prepayment amount of $10.0 million. We may also prepay all or a portion (not less than $5.0 million) of the principal amount of the Deerfield Notes at an optional prepayment price based on a discounted principal amount (during the first three years of the term, subject to a prepayment premium) determined as of the date of prepayment, plus accrued and unpaid interest, plus in the case of a prepayment of the full principal amount of the Deerfield Notes (other than prepayments upon the occurrence of specified transactions relating to a change of control or a substantial sale of assets), all accrued interest that would have accrued between the date of such prepayment and the next anniversary of the note purchase agreement. Contingent upon the closing of the concurrent note offering, we have agreed with Deerfield to amend the terms of the senior secured convertible notes we previously issued to Deerfield to permit us to issue the notes in exchange for the payment of a consent fee of $1.5 million and revised terms for voluntary prepayments of the Deerfield Notes prior to July 2, 2013. In lieu of making any optional or mandatory prepayment in cash, subject to specified limitations, we have the right to convert all or a portion of the principal amount of the Deerfield Notes into, or satisfy all or any portion of the optional prepayment amounts or mandatory prepayment amounts (other than the first $10.0 million of mandatory prepayments required in 2013 and 2014) with, shares of our common stock. Additionally, in lieu of making any payment of accrued and unpaid interest in respect of the Deerfield Notes in cash, subject to specified limitations, we may elect to satisfy any such payment with shares of our common stock. The number of shares of our common stock issuable upon conversion or in settlement of principal and interest obligations will be based upon the discounted trading price of our common stock over a specified trading period. In the event the market price for our common stock is depressed or we do not have a sufficient number of authorized but unissued shares, we may not be able to convert the principal amount of the notes or satisfy our payment obligations in full using shares of our common stock due to restrictions in the agreement on the number of shares we may issue. In addition, the issuance of shares of our common stock to convert the Deerfield Notes or satisfy our payment obligations may result in significant dilution to our stockholders. As a result, we may need to obtain additional funding to satisfy our repayment obligations. There can be no assurance that we will have sufficient funds to repay the Deerfield Notes or satisfy our payment obligations under the note purchase agreement when due or that we will comply with the conditions to our ability to convert the principal amount of the Deerfield Notes into or satisfy our payment obligations with shares of our common stock;

repayment of our loan from SVB: On May 22, 2002, we entered into a loan and security agreement with SVB for an equipment line of credit, on December 21, 2004, December 21, 2006

and December 21, 2007, we amended the loan and security agreement to provide for additional equipment lines of credit and on June 2, 2010, we amended our loan and security agreement with SVB to provide for a new seven-year term loan in an amount of $80.0 million. The principal amount outstanding under the term loan accrues interest at 1.0% per annum, which interest is due and payable monthly. We are required to repay the term loan in one balloon principal payment, representing 100% of the principal balance and accrued and unpaid interest, on May 31, 2017. We are required to repay any advances under an equipment line of credit in 48 equal monthly payments of principal and interest. We have the option to prepay all, but not less than all, of the amounts advanced under the term loan, provided that we pay all unpaid accrued interest thereon that is due through the date of such prepayment and the interest on the entire principal balance of the term loan that would otherwise have been paid after such prepayment date until the maturity date of the term loan. We have the option to prepay without penalty any advance under an equipment line of credit other than advances under a single equipment line of credit, which has a 1.0% prepayment penalty, provided that we pay all unpaid accrued interest thereon that is due through the date of such prepayment. In accordance with the terms of the loan and security agreement, we are also required to maintain an amount equal to at least 100%, but not to exceed 107%, of the outstanding principal balance of the term loan and all equipment lines of credit under the loan and security agreement at all times in one or more accounts with SVB and certain other designated financial institutions as support for our obligations under the loan and security agreement. As a result, the proceeds of the term loan cannot be used to satisfy our other obligations without causing a default under our loan and security agreement with SVB;

the level of payments received under existing collaboration agreements, licensing agreements and other arrangements;

the degree to which we conduct funded development activity on behalf of partners to whom we have out-licensed compounds or programs;

whether we enter into new collaboration agreements, licensing agreements or other arrangements (including, in particular, with respect to cabozantinib) that provide additional capital;

our ability to control costs;

our ability to remain in compliance with, or amend or cause to be waived, financial covenants contained in agreements with third parties;

the amount of our cash and cash equivalents and marketable securities that serve as collateral for bank lines of credit;

future clinical trial results;

our need to expand our product and clinical development efforts;

our ability to share the costs of our clinical development efforts with third parties;

the cost and timing of regulatory approvals;

the cost of clinical and research supplies of our product candidates;

the effect of competing technological and market developments;

the filing, maintenance, prosecution, defense and enforcement of patent claims and other intellectual property rights; and

the cost of any acquisitions of or investments in businesses, products and technologies.

We may seek to raise funds through the sale of equity or debt securities or through external borrowings. In addition, we may enter into additional strategic partnerships, collaborative arrangements or other strategic transactions. It is unclear whether any such partnership, arrangement or transaction will occur, on satisfactory terms or at all, or what the timing and nature of such a partnership, arrangement or transaction may be. The sale of equity or convertible debt securities in the future may be dilutive to our stockholders, and debt-financing arrangements may require us to pledge certain assets and enter into

Table of Contents

covenants that would restrict certain business activities or our ability to incur further indebtedness, and may contain other terms that are not favorable to our stockholders or us. If we are unable to obtain adequate funds on reasonable terms, we may be required to curtail operations significantly or obtain funds by entering into financing, supply or collaboration agreements on unattractive terms or we may be required to relinquish rights to technology or product candidates or to grant licenses on terms that are unfavorable to us.

We may need to obtain additional funding in order to stay in compliance with financial covenants contained in agreements with third parties. The terms of our debt owed to Deerfield and SVB contain covenants or events of default requiring us to maintain specified cash balances. The failure to comply with these covenants could result in an acceleration of the underlying debt obligations. If we cannot raise additional capital in order to remain in compliance with such covenants or if we are unable to renegotiate such covenants and the lender exercises its remedies under the agreement, we would not be able to operate under our current operating plan.

We have a history of net losses. We expect to continue to incur net losses, and we may not achieve or maintain profitability.

We have incurred net losses since inception through 2010. While we were in a net income position of $75.7 million for the year ended December 31, 2011, primarily as a result of the acceleration of revenue recognized under our 2008 collaboration agreement with Bristol-Myers Squibb that terminated in October 2011 and under our 2009 discovery collaboration agreement with Sanofi that terminated in December 2011, we anticipate net losses and negative operating cash flow for the foreseeable future. For the six months ended June 30, 2012, we had a net loss of $62.6 million; as of June 30, 2012, we had an accumulated deficit of $1.2 billion. We have not yet completed the development, including obtaining regulatory approval, of cabozantinib or any other product candidates and, consequently, have not generated revenues from the sale of pharmaceutical products. We have derived substantially all of our revenues to date from collaborative research and development agreements. Revenues from research and development collaborations depend upon continuation of the collaborations, research funding, the achievement of milestones and royalties we earn from any future products developed from the collaborative research. If we are unable to successfully achieve milestones, our collaborators fail to develop successful products or research funding we receive from collaborators decreases, we will not earn the revenues contemplated under such collaborative agreements. The amount of our net losses will depend, in part, on the rate of growth, if any, in our license and contract revenues and on the level of our expenses. These losses have had and will continue to have an adverse effect on our stockholders equity and working capital. Our research and development expenditures and general and administrative expenses have exceeded our revenues through 2010 and for the six months ended June 30, 2012, and we expect to spend significant additional amounts to fund the development of cabozantinib. As a result, we expect to continue to incur substantial operating expenses, and, consequently, we will need to generate significant additional revenues to achieve future profitability. Because of the numerous risks and uncertainties associated with developing drugs, we are unable to predict the extent of any future losses or when we will become profitable, if at all.

We may not realize the expected benefits of our initiatives to control costs.

Managing costs is a key element of our business strategy. Consistent with this element of our strategy, during 2010, we implemented two restructurings that resulted in an overall reduction in our workforce by 386 employees. As a consequence of our decision to focus our proprietary resources and development efforts on the late-stage development and commercialization of cabozantinib, we implemented additional restructurings in both March 2011 and May 2012, that resulted in further reductions to our workforce. The aggregate reduction in headcount from the 2010, 2011 and 2012 restructurings, or the Restructurings, is 422 employees. We have recorded aggregate restructuring

Table of Contents

charges of $43.9 million in connection with the Restructurings and anticipate that we will incur additional restructuring charges related to the exit of all or portions of three of our South San Francisco buildings. These charges will be recorded through the end of the building lease terms, the last of which ends in 2017.

As part of the Restructurings, in 2011 we entered into two sublease agreements for portions of one of our buildings in South San Francisco, California. We are still assessing our ability to sublease portions of our facilities in light of the workforce reductions as well as the potential for sublease income. Estimates for sublease income would require significant assumptions regarding the time required to contract with subtenants, the amount of idle space we would be able to sublease and potential future sublease rates. If we are able to vacate portions of our facilities, we would need to continue to update our estimate of the lease exit costs in our financial statements until we were able to negotiate an exit to the lease or negotiate a sublease for the remaining term of the lease.

If we experience excessive unanticipated inefficiencies or incremental costs in connection with restructuring activities, such as unanticipated inefficiencies caused by reducing headcount, we may be unable to meaningfully realize cost savings and we may incur expenses in excess of what we anticipate. Either of these outcomes could prevent us from meeting our strategic objectives and could adversely impact our results of operations and financial condition.

We are exposed to risks related to foreign currency exchange rates.

Most of our foreign expenses incurred are associated with establishing and conducting clinical trials for cabozantinib. The amount of expenses incurred will be impacted by fluctuations in the currencies of those countries in which we conduct clinical trials. Our agreements with the foreign sites that conduct such clinical trials generally provide that payments for the services provided will be calculated in the currency of that country, and converted into U.S. dollars using various exchange rates based upon when services are rendered or the timing of invoices. When the U.S. dollar weakens against foreign currencies, the U.S. dollar value of the foreign-currency denominated expense increases, and when the U.S. dollar strengthens against these currencies, the U.S. dollar value of the foreign-currency denominated expense decreases. Consequently, changes in exchange rates may affect our financial position and results of operations.

Global credit and financial market conditions could negatively impact the value of our current portfolio of cash equivalents, short-term investments or long-term investments and our ability to meet our financing objectives.

Our cash and cash equivalents are maintained in highly liquid investments with remaining maturities of 90 days or less at the time of purchase. Our short-term and long-term investments consist primarily of readily marketable debt securities with remaining maturities of more than 90 days at the time of purchase. While as of the date of this prospectus supplement we are not aware of any downgrades, material losses, or other significant deterioration in the fair value of our cash equivalents, short-term investments or long-term investments since June 30, 2012, no assurance can be given that a deterioration in conditions of the global credit and financial markets would not negatively impact our current portfolio of cash equivalents or investments or our ability to meet our financing objectives.

Risks Related to Development of Cabozantinib

We are dependent on the successful development and commercialization of cabozantinib.

The success of our business is dependent upon the successful development and commercialization of cabozantinib. As part of our strategy, we intend to dedicate all of our proprietary resources to advance cabozantinib as aggressively as feasible. Our ability to realize the value of our

investment is contingent on, among other things, successful clinical development, regulatory approval and market acceptance of cabozantinib. If we encounter difficulties in the development of cabozantinib due to any of the factors discussed in this Risk Factors section or otherwise, or we do not receive regulatory approval and are unable to commercialize cabozantinib, we will not have the resources necessary to continue our business in its current form.

Clinical testing of cabozantinib and other product candidates is a lengthy, costly, complex and uncertain process and may fail to demonstrate safety and efficacy.

Clinical trials are inherently risky and may reveal that our product candidates are ineffective or have unacceptable toxicity or other side effects that may significantly decrease the likelihood of regulatory approval.

The results of preliminary studies do not necessarily predict clinical or commercial success, and later-stage clinical trials may fail to confirm the results observed in earlier-stage trials or preliminary studies. Although we have established timelines for manufacturing and clinical development of cabozantinib based on existing knowledge of our compounds in development and industry metrics, we may not be able to meet those timelines.

We may experience numerous unforeseen events during, or as a result of, clinical testing that could delay or prevent commercialization of cabozantinib, including:

- cabozantinib may not prove to be efficacious or may cause, or potentially cause, harmful side effects;
- negative or inconclusive clinical trial results may require us to conduct further testing or to abandon projects that we had expected to be promising;
- our competitors may discover or commercialize other compounds or therapies that show significantly improved safety or efficacy compared to cabozantinib;
- patient registration or enrollment in our clinical testing may be lower than we anticipate, resulting in the delay or cancellation of clinical testing; and
- regulators or institutional review boards may withhold authorization of, or delay, suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or their determination that participating patients are being exposed to unacceptable health risks.

If we were to have significant delays in or termination of our clinical testing of cabozantinib as a result of any of the events described above or otherwise, our expenses could increase or our ability to generate revenues from cabozantinib could be impaired, either of which could adversely impact our financial results.

We have limited experience in conducting clinical trials and may not be able to rapidly or effectively continue the further development of cabozantinib or meet current or future requirements of the FDA, including those identified based on our discussions with the FDA. Our planned clinical trials may not begin on time, or at all, may not be completed on schedule, or at all, may not be sufficient for registration of cabozantinib or may not result in an approvable product. For example, as discussed in Risks Related to Regulatory Approval of Cabozantinib-Cabozantinib is subject to a lengthy and uncertain regulatory process that may not result in the necessary regulatory approvals, which could adversely affect our ability to commercialize this product candidate, we were not able to reach a timely agreement with the FDA under a Special Protocol Assessment, or SPA, on the proposed design and analyses of the COMET-2 trial.

Table of Contents

Completion of clinical trials may take several years or more, but the length of time generally varies substantially according to the type, complexity, novelty and intended use of cabozantinib as a product candidate. The duration and the cost of clinical trials may vary significantly over the life of a project as a result of factors relating to the clinical trial, including, among others:

- the number of patients that ultimately participate in the clinical trial;
- the duration of patient follow-up that is appropriate in view of the results;
- the number of clinical sites included in the trials; and
- the length of time required to enroll suitable patient subjects.

Any delay could limit our ability to generate revenues, cause us to incur additional expense and cause the market price of our common stock to decline significantly. Our partners under our collaboration agreements may experience similar risks with respect to the compounds we have out-licensed to them. If any of the events described above were to occur with such programs or compounds, the likelihood of receipt of milestones and royalties under such collaboration agreements could decrease.

If third parties upon which we rely do not perform as contractually required or expected, we may not be able to obtain regulatory approval for or commercialize cabozantinib.

We do not have the ability to independently conduct clinical trials for cabozantinib, and we rely on third parties we do not control such as contract research organizations, medical institutions, clinical investigators and contract laboratories to conduct our clinical trials. If these third parties do not successfully carry out their contractual duties or regulatory obligations or meet expected deadlines, if the third parties need to be replaced or if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for other reasons, our preclinical development activities or clinical trials may be extended, delayed, suspended or terminated, and we may not be able to obtain regulatory approval for or successfully commercialize cabozantinib.

We lack the capability to manufacture compounds for clinical trials and rely on third parties to manufacture cabozantinib, and we may be unable to obtain required material in a timely manner, at an acceptable cost or at a quality level required to receive regulatory approval.

We do not have the manufacturing capabilities or experience necessary to enable us to produce materials for our clinical trials. We rely on collaborators and third-party contractors to produce cabozantinib for clinical testing. These suppliers must comply with applicable regulatory requirements, including the FDA s current Good Manufacturing Practices, or GMP. Our current and anticipated future dependence upon these third-party manufacturers may adversely affect our future profit margins and our ability to develop and commercialize cabozantinib on a timely and competitive basis. These manufacturers may not be able to produce material on a timely basis or manufacture material at the quality or in the quantity required to meet our development timelines and applicable regulatory requirements. We may not be able to maintain or renew our existing third-party manufacturing arrangements, or enter into new arrangements, on acceptable terms, or at all. Our third-party manufacturers could terminate or decline to renew our manufacturing arrangements based on their own business priorities, at a time that is costly or inconvenient for us. If we are unable to contract for the production of materials in sufficient quantity and of sufficient quality on acceptable terms, our clinical trials may be delayed. Delays in preclinical or clinical testing could delay the initiation of clinical trials.

Our third-party manufacturers may not be able to comply with the GMP regulations, other applicable FDA regulatory requirements or similar regulations applicable outside of the United States. Additionally, if we are required to enter into new supply arrangements, we may not be able to obtain

Table of Contents

approval from the FDA of any alternate supplier in a timely manner, or at all, which could delay or prevent the clinical development and commercialization of cabozantinib. Failure of our third-party manufacturers or us to obtain approval from the FDA or to comply with applicable regulations could result in sanctions being imposed on us, including fines, civil penalties, delays in or failure to grant marketing approval of cabozantinib, injunctions, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products and compounds, operating restrictions and criminal prosecutions, any of which could have a significant adverse affect on our business.

Materials necessary to manufacture cabozantinib may not be available on commercially reasonable terms, or at all, which may delay its development and commercialization.

Some of the materials necessary for the manufacture of cabozantinib may, from time to time, be available either in limited quantities, or from a limited number of manufacturers, or both. Our contract manufacturers need to obtain these materials for our clinical trials and, potentially, for commercial distribution when and if we obtain marketing approval for cabozantinib. Suppliers may not sell us these materials at the time we need them or on commercially reasonable terms. If we are unable to obtain the materials needed to conduct our clinical trials, product testing and potential regulatory approval could be delayed, adversely affecting our ability to develop cabozantinib. Similarly, if we are unable to obtain critical manufacturing materials after regulatory approval has been obtained, the commercial launch of cabozantinib could be delayed or there could be a shortage in supply, which could materially affect our ability to generate revenues from sales of cabozantinib. If suppliers increase the price of manufacturing materials, the price for cabozantinib may increase, which may make it less competitive in the marketplace. If it becomes necessary to change suppliers for any of these materials or if any of our suppliers experience a shutdown or disruption at the facilities used to produce these materials, due to technical, regulatory or other reasons, it could harm our ability to manufacture cabozantinib.

Risks Related to Our Relationships with Third Parties

We are dependent upon our collaborations with major companies, which subjects us to a number of risks.

We have established collaborations with leading pharmaceutical and biotechnology companies, including Bristol-Myers Squibb, Sanofi, Genentech, Inc. (a wholly- owned member of the Roche Group), GlaxoSmithKline, Merck (known as MSD outside of the United States and Canada) and Daiichi Sankyo Company Limited, or Daiichi Sankyo, for the development and ultimate commercialization of a significant number of compounds generated from our research and development efforts. We continue to pursue collaborations for selected unpartnered preclinical and clinical programs and compounds. Our dependence on our relationships with existing collaborators for the development and commercialization of our compounds subjects us to, and our dependence on future collaborators for development and commercialization of additional compounds will subject us to, a number of risks, including:

- we are not able to control the amount and timing of resources that our collaborators will devote to the development or commercialization of drug candidates or to their marketing and distribution;
- we may not be able to control the amount and timing of resources that our potential future collaborators may devote to the development or commercialization of drug candidates or to their marketing and distribution;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a drug candidate, repeat or conduct new clinical trials or require a new formulation of a drug candidate for clinical testing;
- disputes may arise between us and our collaborators that result in the delay or termination of the research, development or commercialization of our drug candidates or that result in costly litigation or arbitration that diverts management s attention and resources;

Table of Contents

collaborators may experience financial difficulties;

collaborators may not be successful in their efforts to obtain regulatory approvals in a timely manner, or at all;

collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation;

business combinations or significant changes in a collaborator s business strategy may adversely affect a collaborator s willingness or ability to complete its obligations under any arrangement;

a collaborator could independently move forward with a competing drug candidate developed either independently or in collaboration with others, including our competitors;

we may be precluded from entering into additional collaboration arrangements with other parties in an area or field of exclusivity;

future collaborators may require us to relinquish some important rights, such as marketing and distribution rights; and

collaborations may be terminated (as occurred with respect to cabozantinib and XL281, which were previously subject to our 2008 collaboration agreement with Bristol-Myers Squibb, and with respect to our 2009 discovery collaboration with Sanofi, which was terminated in December 2011) or allowed to expire, which would delay, and may increase the cost of development of, our drug candidates.

If any of these risks materialize, our product development efforts could be delayed and otherwise adversely affected, which could adversely impact our business, operating results and financial condition.

If we are unable to continue current collaborations and achieve milestones or royalties, our revenues would suffer.

We have derived substantially all of our revenues to date from collaborative research and development agreements. Revenues from research and development collaborations depend upon continuation of the collaborations, the achievement of milestones and royalties we earn from any future products developed from the collaborative research. If we are unable to successfully achieve milestones or royalties, or our collaborators fail to develop successful products, we will not earn the revenues contemplated under such collaborative agreements.

If any of these agreements is terminated early (as occurred with respect to cabozantinib and XL281, which were previously subject to our 2008 collaboration agreement with Bristol-Myers Squibb, and with respect to our 2009 discovery collaboration with Sanofi, which was terminated in December 2011), whether unilaterally or by mutual agreement, our revenues could suffer. Most of our collaboration agreements contain early termination provisions. In addition, from time to time we review and assess certain aspects of our collaborations, partnerships and agreements and may amend or terminate, either by mutual agreement or pursuant to any applicable early termination provisions, such collaborations, partnerships or agreements if we deem them to be no longer in our economic or strategic interests. We may not be able to enter into new collaboration agreements on similar or superior financial terms to offset the loss of revenues from the termination or expiration of any of our existing or recently terminated arrangements.

We may be unable to establish collaborations for selected preclinical and clinical compounds.

Our strategy includes the pursuit of new collaborations with leading pharmaceutical and biotechnology companies for the development and ultimate commercialization of selected preclinical and clinical programs and compounds, particularly those drug candidates for which we believe that the

Table of Contents

capabilities and resources of a partner can accelerate development and help to fully realize their therapeutic and commercial potential. We face significant competition in seeking appropriate collaborators, and these collaborations are complex and time consuming to negotiate and document. We may not be able to negotiate additional collaborations on acceptable terms, or at all. We are unable to predict when, if ever, we will enter into any additional collaborations because of the numerous risks and uncertainties associated with establishing additional collaborations. If we are unable to negotiate additional collaborations, we may not be able to realize value from a particular drug candidate, particularly those drug candidates as to which we believe a broad development program is appropriate or for which we have determined not to continue to utilize our own resources to develop. As a result, our revenues, capital resources and product development efforts could be adversely affected.

Risks Related to Regulatory Approval of Cabozantinib

Cabozantinib is subject to a lengthy and uncertain regulatory process that may not result in the necessary regulatory approvals, which could adversely affect our ability to commercialize this product candidate.

Cabozantinib, as well as the activities associated with the research, development and commercialization of the product candidate, are subject to extensive regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other countries. Failure to obtain regulatory approval for cabozantinib would prevent us from commercializing this product candidate. We have not received regulatory approval to market cabozantinib in any jurisdiction and have only limited experience in preparing and filing the applications necessary to gain regulatory approvals. The process of obtaining regulatory approvals is expensive, and often takes many years, if approval is obtained at all, and can vary substantially based upon the type, complexity and novelty of the product candidates involved. Before an NDA can be submitted to the FDA, the product candidate must undergo extensive clinical trials, which can take many years and require substantial expenditures.

Our EXAM phase 3 trial of cabozantinib as a potential treatment for medullary thyroid cancer has been conducted under a SPA with the FDA. A SPA is designed to facilitate the FDA s review and provide feedback on the proposed design and size of clinical trials that are intended to form the primary basis for determining a product candidate s efficacy. If agreement is reached with the FDA, a SPA agreement documents the terms and conditions under which the design of the subject trial will be adequate for submission of the efficacy and human safety portion of an NDA. However, there are circumstances under which we may not receive the benefits of a SPA, notably if the FDA subsequently identifies a substantial scientific issue essential to determining the product candidate s safety or efficacy, and we may be required to conduct significant additional development in order to obtain regulatory approval notwithstanding the SPA. We completed the submission of our rolling NDA based on the data from our EXAM trial with the FDA in May 2012. On July 30, 2012, we announced that the FDA has accepted our NDA for filing and granted a Priority Review designation with a stated action date of November 29, 2012. However, our NDA may be subject to delay or lack of approval, including delay or lack of approval based on potential feedback from an FDA Advisory Committee.

In December 2011, we initiated COMET-2, our first phase 3 pivotal trial of cabozantinib in patients with metastatic castration-resistant prostate cancer, with pain response as the primary efficacy endpoint for the trial. We were not able to reach a timely agreement with the FDA for a SPA on the proposed design and analysis of the COMET-2 trial. We originally submitted the proposed protocol for this trial using primary endpoints of pain reduction and bone scan response to the FDA in June 2011 with a request for a SPA. The FDA s final response prior to our discontinuation of the SPA process, which we received in October 2011, raised the following concerns regarding the COMET-2 trial design in the context of its consideration of a SPA for the trial, among other comments:

A concern about the ability to maintain blinding of the trial due to differences in toxicity profiles between cabozantinib and mitoxantrone.

Table of Contents

A view that the assumed magnitude of pain improvement is modest and could represent a placebo effect or be attained with less toxicity by opioid therapy.

A view that symptomatic improvement should be supported by evidence of anti-tumor activity, an acceptable safety profile and lack of survival decrement. The FDA also expressed the view that if the effect that we believe cabozantinib will have on pain is mediated by anti-tumor activity, that anti-tumor activity should translate into an improvement in overall survival.

A recommendation that if we use pain response as a primary efficacy endpoint, that we conduct two adequate and well-controlled trials to demonstrate effectiveness as, according to the FDA, a conclusion based on two persuasive studies will always be more secure. The FDA advised that for a single randomized trial to support a new drug application, the trial must be well designed, well conducted, internally consistent and provide statistically persuasive efficacy findings so that a second trial would be ethically or practically impossible to perform.

In the context of its consideration of a SPA for the COMET-2 trial, the FDA also recommended that overall survival be the primary efficacy endpoint. The final FDA response prior to our discontinuation of the SPA process stated that we could choose to conduct the trial in the absence of a SPA agreement. We elected to proceed with initiation of the COMET-2 trial and the COMET-1 trial, and to discontinue further attempts to secure a SPA agreement with respect to the COMET-2 trial. We initiated the COMET-2 trial with a pain palliation endpoint in December 2011 and the COMET-1 trial with an overall survival endpoint in May 2012.

Any clinical trial may fail to produce results satisfactory to the FDA. For example, the FDA could determine that the design of a clinical trial is inadequate to produce reliable results. The regulatory process also requires preclinical testing, and data obtained from preclinical and clinical activities are susceptible to varying interpretations. The FDA has substantial discretion in the approval process and may refuse to approve any NDA (regardless of prior receipt of a SPA) or decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. For example, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent regulatory approval of cabozantinib.

In addition, delays or rejections may be encountered based upon changes in regulatory policy for product approval during the period of product development and regulatory agency review. Changes in regulatory approval policy, regulations or statutes or the process for regulatory review during the development or approval periods of cabozantinib may cause delays in the approval or rejection of an application.

Even if the FDA or a comparable authority in another country approves cabozantinib, the approval may impose significant restrictions on the indicated uses, conditions for use, labeling, distribution, advertising, promotion, marketing and/or production of cabozantinib and may impose ongoing requirements for post- approval studies, including additional research and development and clinical trials. These agencies also may impose various civil or criminal sanctions for failure to comply with regulatory requirements, including withdrawal of product approval.

Risks Related to Commercialization of Cabozantinib

The commercial success of cabozantinib will depend upon the degree of market acceptance of the product candidate among physicians, patients, health care payors, and the medical community.*

Our ability to commercialize cabozantinib, if it is approved for commercial sale, will be highly dependent upon the extent to which the product candidate gains market acceptance among physicians; patients; health care payors, such as Medicare and Medicaid; and the medical community.

Table of Contents

If cabozantinib does not achieve an adequate level of acceptance, we may not generate adequate product revenues, if at all, and we may not become profitable. The degree of market acceptance of cabozantinib, if approved for commercial sale, will depend upon a number of factors, including:

- the effectiveness, or perceived effectiveness, of cabozantinib in comparison to competing products;
- the existence of any significant side effects of cabozantinib, as well as their severity in comparison to those of any competing products;
- potential advantages or disadvantages in relation to alternative treatments;
- the timing of market entry relative to competitive treatments;
- indications for which cabozantinib is approved;
- the ability to offer cabozantinib for sale at competitive prices;
- relative convenience and ease of administration;
- the strength of marketing and distribution support; and
- sufficient third-party coverage or reimbursement.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell cabozantinib, we may be unable to generate product revenues.

We have no experience as a company in the sales and distribution of pharmaceutical products and do not have a sales organization. Developing a sales force could be expensive and time-consuming, could delay any product launch, including our potential launch of cabozantinib for the treatment of medullary thyroid cancer, and we may never be able to develop this capacity. To the extent that we enter into arrangements with third parties to provide sales, marketing and distribution services, our product revenues may be lower than if we market and sell cabozantinib ourselves. If we are unable to establish adequate sales, marketing and distribution capabilities, independently or with others, we may not be able to generate product revenues.

If we are unable to obtain adequate coverage and reimbursement from third-party payors for cabozantinib, our revenues and prospects for profitability will suffer.

Our ability to commercialize cabozantinib will be highly dependent on the extent to which coverage and reimbursement for the product candidate will be available from third-party payors, including governmental payors, such as Medicare and Medicaid, and private health insurers. Many patients will not be capable of paying themselves for cabozantinib and will rely on third-party payors to pay for, or subsidize, their medical needs. If third-party payors do not provide coverage or reimbursement for cabozantinib, our revenues and prospects for profitability will suffer. In addition, even if third-party payors provide some coverage or reimbursement for cabozantinib, the availability of such coverage or reimbursement for prescription drugs under private health insurance and managed care plans often varies based on the type of contract or plan purchased.

Another factor that may affect the pricing of drugs is proposed congressional action regarding drug reimportation into the United States. For example, the Medicare Prescription Drug, Improvement and Modernization Act of 2003 gives discretion to the Secretary of Health and Human Services to allow drug reimportation into the United States under some circumstances from foreign countries, including countries where the drugs are sold at a lower price than in the United States. Proponents of drug reimportation may attempt to pass legislation, which would allow direct reimportation under certain circumstances. If legislation or regulations were passed allowing the reimportation of drugs, it could decrease the price we receive for cabozantinib, thereby negatively affecting our revenues and prospects for profitability.

Table of Contents

In addition, in some foreign countries, particularly the countries in the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, price negotiations with governmental authorities can take six to twelve months or longer after the receipt of regulatory marketing approval for a product. To obtain reimbursement and/or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost effectiveness of cabozantinib to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in the commercialization of cabozantinib. Third-party payors are challenging the prices charged for medical products and services, and many third-party payors limit reimbursement for newly approved health care products. In particular, third-party payors may limit the indications for which they will reimburse patients who use cabozantinib. Cost-control initiatives could decrease the price we might establish for cabozantinib, which would result in lower product revenues to us.

Current healthcare laws and regulations and future legislative or regulatory reforms to the healthcare system may affect our ability to sell cabozantinib profitably.

The U.S. and some foreign jurisdictions are considering or have enacted a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our products profitably. Among policy makers and payors in the U.S. and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the U.S., the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively, PPACA, became law in the U.S. PPACA substantially changes the way healthcare is financed by both governmental and private insurers and significantly affects the pharmaceutical industry. The United States Supreme Court heard a constitutional challenge to the PPACA and in June 2012 held that the PPACA is constitutional. However, states are allowed to opt out of the expansion of eligibility criteria for Medicaid under the PPACA. We anticipate 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 an additional downward pressure on the price that we receive for any approved product, and could seriously harm our business. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. Insurers may also refuse to provide any coverage of uses of approved products for medical indications other than those for which the FDA has granted market approvals. As a result, significant uncertainty exists as to whether and how much third-party payors will reimburse for newly-approved drugs, which in turn will put pressure on the pricing of drugs.

We also cannot be certain that cabozantinib will successfully be placed on the list of drugs covered by particular health plan formularies, nor can we predict the negotiated price for cabozantinib, which will be determined by market factors. Many states have also created preferred drug lists and include drugs on those lists only when the manufacturers agree to pay a supplemental rebate. If cabozantinib is not included on these preferred drug lists, physicians may not be inclined to prescribe it to their Medicaid patients, thereby diminishing the potential market for cabozantinib.

As a result of the PPACA and the trend towards cost-effectiveness criteria and managed healthcare in the United States, third-party payors are increasingly attempting to contain healthcare costs by limiting both coverage and the level of reimbursement of new drugs. They may use tiered reimbursement and may adversely affect demand for our products by placing them in an expensive tier. They may also refuse to provide any coverage of uses of approved products for medical indications other than those for which the FDA has granted market approvals. As a result, significant uncertainty exists as to whether and how much third-party payors will reimburse for newly-approved drugs, which in turn will put pressure on the pricing of drugs. Further, we do not have experience in ensuring approval by applicable third-party payors outside of the United States for coverage and

Table of Contents

reimbursement of cabozantinib. We also anticipate pricing pressures in connection with the sale of our products due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative proposals.

Our competitors may develop products and technologies that make cabozantinib obsolete.

The biotechnology industry is highly fragmented and is characterized by rapid technological change. In particular, the area of kinase-targeted therapies is a rapidly evolving and competitive field. We face, and will continue to face, intense competition from biotechnology and pharmaceutical companies, as well as academic research institutions, clinical reference laboratories and government agencies that are pursuing research activities similar to ours. Some of our competitors have entered into collaborations with leading companies within our target markets, including some of our existing collaborators. Some of our competitors are further along in the development of their products than we are. In addition, delays in the development of cabozantinib could allow our competitors to bring products to market before us, which would impair our ability to commercialize cabozantinib. Our future success will depend upon our ability to maintain a competitive position with respect to technological advances. Any products that are developed through our technologies will compete in highly competitive markets. Further, our competitors may be more effective at using their technologies to develop commercial products. Many of the organizations competing with us have greater capital resources, larger research and development staff and facilities, more experience in obtaining regulatory approvals and more extensive product manufacturing and marketing capabilities than we do. As a result, our competitors may be able to more easily develop technologies and products that would render our technologies and products, and those of our collaborators, obsolete and noncompetitive. There may also be drug candidates of which we are not aware at an earlier stage of development that may compete with cabozantinib. In addition, if cabozantinib is successfully developed, it may compete with existing therapies that have long histories of use, such as chemotherapy and radiation treatments in cancer indications. Examples of potential competition for cabozantinib include AstraZeneca s RET, VEGFR and EGFR inhibitor, vandetanib, Algeta s development-stage alpha-pharmaceutical Alpharadin (Radium-223), other VEGF pathway inhibitors, including Genentech s bevacizumab, and other MET inhibitors, including Pfizer s crizotinib, ArQule s tivantinib (ARQ197), GlaxoSmithKline s foretinib (XL880), and Genentech s onartuzumab.

We may not be able to manufacture cabozantinib in commercial quantities, which would prevent us from commercializing the product candidate.

To date, cabozantinib has been manufactured in small quantities for preclinical and clinical trials. If cabozantinib is approved by the FDA or other regulatory agencies for commercial sale, we will need to manufacture it in larger quantities. We may not be able to successfully increase the manufacturing capacity, whether in collaboration with third-party manufacturers or on our own, for cabozantinib in a timely or economic manner, or at all. Significant scale-up of manufacturing may require additional validation studies, which the FDA must review and approve. If we are unable to successfully increase the manufacturing capacity for cabozantinib, the regulatory approval or commercial launch of the product candidate may be delayed or there may be a shortage in supply. Cabozantinib requires precise, high- quality manufacturing. The failure to achieve and maintain these high manufacturing standards, including the incidence of manufacturing errors, could result in patient injury or death, product recalls or withdrawals, delays or failures in product testing or delivery, cost overruns or other problems that could seriously hurt our business.

Risks Related to Our Intellectual Property

If we are unable to adequately protect our intellectual property, third parties may be able to use our technology, which could adversely affect our ability to compete in the market.

Our success will depend in part upon our ability to obtain patents and maintain adequate protection of the intellectual property related to our technologies and products. The patent positions of

biotechnology companies, including our patent position, are generally uncertain and involve complex legal and factual questions. We will be able to protect our intellectual property rights from unauthorized use by third parties only to the extent that our technologies are covered by valid and enforceable patents or are effectively maintained as trade secrets. We will continue to apply for patents covering our technologies and products as and when we deem appropriate. However, these applications may be challenged or may fail to result in issued patents. In addition, because patent applications can take many years to issue, there may be pending applications, unknown to us, which may later result in issued patents that cover the production, manufacture, commercialization or use of our product candidates. Our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from practicing our technologies or from developing competing products. Furthermore, others may independently develop similar or alternative technologies or design around our patents. In addition, our patents may be challenged or invalidated or may fail to provide us with any competitive advantages, if, for example, others were the first to invent or to file patent applications for these inventions.

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States, and many companies have encountered significant problems in protecting and defending such rights in foreign jurisdictions. Many countries, including certain countries in Europe, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties (for example, the patent owner has failed to work the invention in that country or the third party has patented improvements). In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of the patent. Compulsory licensing of life-saving drugs is also becoming increasingly popular in developing countries either through direct legislation or international initiatives. Such compulsory licenses could be extended to include some of our product candidates, which could limit our potential revenue opportunities. Moreover, the legal systems of certain countries, particularly certain developing countries, do not favor the aggressive enforcement of patent and other intellectual property protection, which makes it difficult to stop infringement. We rely on trade secret protection for our confidential and proprietary information. We have taken security measures to protect our proprietary information and trade secrets, but these measures may not provide adequate protection. While we seek to protect our proprietary information by entering into confidentiality agreements with employees, collaborators and consultants, we cannot assure you that our proprietary information will not be disclosed, or that we can meaningfully protect our trade secrets. In addition, our competitors may independently develop substantially equivalent proprietary information or may otherwise gain access to our trade secrets.

Litigation or third-party claims of intellectual property infringement could require us to spend substantial time and money and adversely affect our ability to develop and commercialize products.

Our commercial success depends in part upon our ability to avoid infringing patents and proprietary rights of third parties and not to breach any licenses that we have entered into with regard to our technologies. Other parties have filed, and in the future are likely to file, patent applications covering genes and gene fragments, techniques and methodologies relating to model systems and products and technologies that we have developed or intend to develop. If patents covering technologies required by our operations are issued to others, we may have to obtain licenses from third parties, which may not be available on commercially reasonable terms, or at all, and may require us to pay substantial royalties, grant a cross-license to some of our patents to another patent holder or redesign the formulation of a product candidate so that we do not infringe third-party patents, which may be impossible to obtain or could require substantial time and expense.

Third parties may accuse us of employing their proprietary technology without authorization. In addition, third parties may obtain patents that relate to our technologies and claim that use of such

technologies infringes on their patents. Regardless of their merit, such claims could require us to incur substantial costs, including the diversion of management and technical personnel, in defending ourselves against any such claims or enforcing our patents. In the event that a successful claim of infringement is brought against us, we may be required to pay damages and obtain one or more licenses from third parties. We may not be able to obtain these licenses at a reasonable cost, or at all. Defense of any lawsuit or failure to obtain any of these licenses could adversely affect our ability to develop and commercialize products.

We may be subject to damages resulting from claims that we, our employees or independent contractors have wrongfully used or disclosed alleged trade secrets of their former employers.

Many of our employees and independent contractors were previously employed at universities, other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We may be subject to claims that these employees, independent contractors or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and divert management s attention. If we fail in defending such claims, in addition to paying money claims, we may lose valuable intellectual property rights or personnel. A loss of key research personnel and/or their work product could hamper or prevent our ability to commercialize certain product candidates, which could severely harm our business.

Risks Related to Employees and Location

The loss of key personnel or the inability to retain and, where necessary, attract additional personnel could impair our ability to expand our operations.

We are highly dependent upon the principal members of our management and scientific staff, the loss of whose services might adversely impact the achievement of our objectives and the continuation of existing collaborations. Also, we may not have sufficient personnel to execute our business plan. Retaining and, where necessary, recruiting qualified clinical and scientific personnel will be critical to support activities related to advancing our clinical and preclinical development programs, and supporting our collaborative arrangements and our internal proprietary research and development efforts. The Restructurings could have an adverse impact on our ability to retain and recruit qualified personnel. Competition is intense for experienced clinical personnel, and we may be unable to retain or recruit clinical personnel with the expertise or experience necessary to allow us to pursue collaborations, develop our products and core technologies or expand our operations to the extent otherwise possible. Further, all of our employees are employed at will and, therefore, may leave our employment at any time.

Our collaborations with outside scientists may be subject to restriction and change.

We work with scientific and clinical advisors and collaborators at academic and other institutions that assist us in our research and development efforts. These advisors and collaborators are not our employees and may have other commitments that limit their availability to us. Although these advisors and collaborators generally agree not to do competing work, if a conflict of interest between their work for us and their work for another entity arises, we may lose their services. In such a circumstance, we may lose work performed by them, and our development efforts with respect to the matters on which they were working may be significantly delayed or otherwise adversely affected. In addition, although our advisors and collaborators sign agreements not to disclose our confidential information, it is possible that valuable proprietary knowledge may become publicly known through them.

Table of Contents

Our headquarters are located near known earthquake fault zones, and the occurrence of an earthquake or other disaster could damage our facilities and equipment, which could harm our operations.

Our headquarters are located in South San Francisco, California, and therefore our facilities are vulnerable to damage from earthquakes. We do not carry earthquake insurance. We are also vulnerable to damage from other types of disasters, including fire, floods, power loss, communications failures, terrorism and similar events since any insurance we may maintain may not be adequate to cover our losses. If any disaster were to occur, our ability to operate our business at our facilities could be seriously, or potentially completely, impaired. In addition, the unique nature of our research activities could cause significant delays in our programs and make it difficult for us to recover from a disaster. Accordingly, an earthquake or other disaster could materially and adversely harm our ability to conduct business.

Security breaches may disrupt our operations and harm our operating results.

Our network security and data recovery measures may not be adequate to protect against computer viruses, break-ins, and similar disruptions from unauthorized tampering with our computer systems. The misappropriation, theft, sabotage or any other type of security breach with respect to any of our proprietary and confidential information that is electronically stored, including research or clinical data, could have a material adverse impact on our business, operating results and financial condition. Additionally, any break-in or trespass of our facilities that results in the misappropriation, theft, sabotage or any other type of security breach with respect to our proprietary and confidential information, including research or clinical data, or that results in damage to our research and development equipment and assets could have a material adverse impact on our business, operating results and financial condition.

Risks Related to Environmental and Product Liability

We use hazardous chemicals and radioactive and biological materials in our business. Any claims relating to improper handling, storage or disposal of these materials could be time consuming and costly.

Our research and development processes involve the controlled use of hazardous materials, including chemicals and radioactive and biological materials. Our operations produce hazardous waste products. We cannot eliminate the risk of accidental contamination or discharge and any resultant injury from these materials. Federal, state and local laws and regulations govern the use, manufacture, storage, handling and disposal of hazardous materials. We may face liability for any injury or contamination that results from our use or the use by third parties of these materials, and such liability may exceed our insurance coverage and our total assets. Compliance with environmental laws and regulations may be expensive, and current or future environmental regulations may impair our research, development and production efforts.

In addition, our collaborators may use hazardous materials in connection with our collaborative efforts. In the event of a lawsuit or investigation, we could be held responsible for any injury caused to persons or property by exposure to, or release of, these hazardous materials used by these parties. Further, we may be required to indemnify our collaborators against all damages and other liabilities arising out of our development activities or products produced in connection with these collaborations.

We face potential product liability exposure far in excess of our limited insurance coverage.

We may be held liable if any product we or our collaborators develop causes injury or is found otherwise unsuitable during product testing, manufacturing, marketing or sale. Regardless of merit or eventual outcome, product liability claims could result in decreased demand for our product candidates,

Table of Contents

injury to our reputation, withdrawal of patients from our clinical trials, substantial monetary awards to trial participants and the inability to commercialize any products that we may develop. These claims might be made directly by consumers, health care providers, pharmaceutical companies or others selling or testing our products. We have obtained limited product liability insurance coverage for our clinical trials in the amount of $10.0 million per occurrence and $10.0 million in the aggregate. However, our insurance may not reimburse us or may not be sufficient to reimburse us for expenses or losses we may suffer. Moreover, if insurance coverage becomes more expensive, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If we obtain marketing approval for cabozantinib, we intend to expand our insurance coverage to include the sale of commercial products, but we may be unable to obtain commercially reasonable product liability insurance for any products approved for marketing. On occasion, juries have awarded large judgments in class action lawsuits for claims based on drugs that had unanticipated side effects. In addition, the pharmaceutical and biotechnology industries, in general, have been subject to significant medical malpractice litigation. A successful product liability claim or series of claims brought against us could harm our reputation and business and would decrease our cash reserves.

Risks Related to Our Common Stock

We expect that our quarterly results of operations will fluctuate, and this fluctuation could cause our stock price to decline, causing investor losses.

Our quarterly operating results have fluctuated in the past and are likely to fluctuate in the future. A number of factors, many of which we cannot control, could subject our operating results to volatility, including:

- the progress and scope of our research and development activities;
- recognition of up-front licensing or other fees or revenues;
- payments of non-refundable up-front or licensing fees, or payment for cost-sharing expenses, to third parties;
- acceptance of our technologies and platforms;
- the success rate of our efforts leading to milestone payments and royalties;
- the introduction of new technologies or products by our competitors;
- the timing and willingness of collaborators to further develop or, if approved, commercialize our product out-licensed to them;
- our ability to enter into new collaborative relationships;
- the termination or non-renewal of existing collaborations;
- the timing and amount of expenses incurred for clinical development and manufacturing of cabozantinib;

adjustments to expenses accrued in prior periods based on management s estimates after the actual level of activity relating to such expenses becomes more certain;

the impairment of acquired goodwill and other assets;

the impact of our restructurings; and

general and industry-specific economic conditions that may affect our collaborators research and development expenditures.

A large portion of our expenses, including expenses for facilities, equipment and personnel, are relatively fixed in the short term. If we fail to achieve anticipated levels of revenues, whether due to the

Table of Contents

expiration or termination of existing contracts, our failure to obtain new contracts, our inability to meet milestones or for other reasons, we may not be able to correspondingly reduce our operating expenses, which could significantly harm our operating results for a particular fiscal period.

Due to the possibility of fluctuations in our revenues and expenses, we believe that quarter-to-quarter comparisons of our operating results are not a good indication of our future performance. As a result, in some future quarters, our operating results may not meet the expectations of securities analysts and investors, which could result in a decline in the price of our common stock.

Our stock price may be extremely volatile.

The trading price of our common stock has been highly volatile, and we believe the trading price of our common stock will remain highly volatile and may fluctuate substantially due to factors such as the following, many of which we cannot control:

- adverse results or delays in our or our collaborators clinical trials;
- announcement of FDA approval or non-approval, or delays in the FDA review process, of cabozantinib or our collaborators product candidates or those of our competitors or actions taken by regulatory agencies with respect to our, our collaborators or our competitors clinical trials;
- the timing of achievement of our clinical, regulatory, partnering and other milestones, such as the commencement of clinical development, the completion of a clinical trial, the filing for regulatory approval or the establishment of collaborative arrangements for one or more of our out-licensed programs and compounds;
- actions taken by regulatory agencies with respect to cabozantinib or our clinical trials for cabozantinib;
- the announcement of new products by our competitors;
- quarterly variations in our or our competitors results of operations;