Cyclacel Pharmaceuticals, Inc.
Form 10-K
March 16, 2007

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

FORM 10-K

(Mark One)

Annual Report Pursuant to Section 13 or 15(d) of
the Securities Exchange Act of 1934

For the year ended December 31, 2006

OR

Transition Report Pursuant to Section 13 or 15(d) of
the Securities Exchange Act of 1934B

Commission file number 0-50626

CYCLACEL PHARMACEUTICALS, INC.
(Exact name of Registrant as Specified in Its Charter)

Delaware (State or Other Jurisdiction of Incorporation or Organization)	91-1707622 (I.R.S. Employer Identification No.)
200 Connell Drive Suite 1500, Berkeley Heights, NJ 07922 (Address of principal executive offices)	07078 (Zip Code)

Registrant's telephone number, including area code: (908) 517-7330

Securities registered under Section 12(b) of the Exchange Act:

Title of Each Class	Name of Each Exchange on Which Registered
Common Stock, $0.001 par value	The NASDAQ Stock Market LLC
Preferred Stock, $0.001 par value	The NASDAQ Stock Market LLC

Indicate by check mark if the registrant is a well known seasoned issuer, as defined in Rule 405 of the Securities Act.
Yes No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange Act. Yes No

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendments to this Form 10-K .

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer or a non-accelerated filer. See definition of 'accelerated filer and large accelerated filer' as defined in Rule 12b-2 of the Exchange Act (Check one):

Large accelerated filer Accelerated filer Non-accelerated filer

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes No

As of March 14, 2007 there were 20,407,621 shares of the registrant's common stock outstanding.

Table of Contents

DOCUMENTS INCORPORATED BY REFERENCE

The following documents (or parts thereof) are incorporated by reference into the following parts of this Form 10-K: Certain information required in Part III of this Annual Report on Form 10-K is incorporated from the Registrant's Proxy Statement for the Annual Meeting of Stockholders to be held on May 21, 2007.

TABLE OF CONTENTS

Table of Contents

PART I

Item 1. Business

In this report, 'Cyclacel,' the 'Company,' 'we', 'us' and 'our' refer to Cyclacel Pharmaceuticals, Inc.

General

Cyclacel Pharmaceuticals, Inc. ('Cyclacel', or the 'Company') was incorporated in the state of Delaware in 1996 and is headquartered in Berkeley Heights, New Jersey with research facilities located in Dundee, Scotland and Cambridge, England. Cyclacel is a development-stage biopharmaceutical company dedicated to the discovery, development and eventual commercialization of novel, mechanism-targeted drugs to treat human cancers and other serious disorders. As a development stage enterprise, substantially all efforts of the Company to date have been devoted to performing research and development, conducting clinical trials, developing and acquiring intellectual properties, raising capital and recruiting and training personnel.

Recent Corporate History

On March 27, 2006, Xcyte Therapies Inc. ('Xcyte') completed a Stock Purchase Agreement (the 'Stock Purchase Agreement') with Cyclacel Group plc ('Group'), a public company organized under the laws of England and Wales in which Xcyte agreed to purchase from Group all of the capital stock of Cyclacel Limited ('Limited'), a private limited company organized under the laws of England and Wales and a wholly-owned subsidiary of Group (the 'Stock Purchase'). Under the terms of the Stock Purchase Agreement, Xcyte issued 7,761,453 shares of common stock to Group which, after giving effect to the transaction, represented 79.7% of the outstanding shares of Xcyte's common stock. Limited became Xcyte's wholly owned subsidiary. Xcyte changed its name to Cyclacel Pharmaceuticals, Inc. The transaction has been accounted for as a reverse acquisition under the purchase method of accounting for business combinations in accordance with accounting principles generally accepted in the United States and Limited is considered the acquiring company for accounting purposes. Accordingly, the purchase price has been allocated among the fair values of the assets and liabilities of Xcyte, while the historical results of Limited are reflected in the results of the Company. On March 27, 2006, Group effected a members' voluntary liquidation in accordance with its memorandum and articles of association and the applicable laws of England and Wales, which has resulted in the distribution of its assets, including the Xcyte common stock it received in the Stock Purchase, to its shareholders and creditors.

Prior to the Stock purchase, on March 24, 2006 Xcyte completed an Asset Purchase Agreement (the 'Asset Purchase Agreement') with Invitrogen Corporation, a Delaware corporation ('Invitrogen'), in which Invitrogen agreed to purchase Xcyte's T cell expansion technology known as the 'Xcellerate Process' in exchange for $5 million (the 'Asset Sale'). The assets subject to the agreement included intellectual property, the clinical data generated by Xcyte in the course of six clinical trials of the lead product, Xcellerated T Cells, as well as raw materials and equipment.

On March 16, 2006, Xcyte stockholders approved a one-for-ten reverse stock split of its common stock. The reverse stock split occurred immediately prior to the completion of the Stock Purchase. All information in this report relating to the number of shares, price per share, and per share amounts of common stock are presented on a post-split basis.

On April 26, 2006, Cyclacel raised net proceeds of $42.6 million through a private placement of common stock and common stock purchase warrants. We issued 6.43 million shares of our common stock at a price of $7.00 per share. In addition, 2.57 million seven-year common stock purchase warrants were issued to the investors granting them the right to purchase Cyclacel's common stock at a price of $7.00 per share.

On February 16, 2007, Cyclacel raised net proceeds of $33.3 million through a registered direct offering of common stock and common stock purchase warrants. We issued 4.25 million shares of our common stock at a price of $8.44 per share. In addition, 1.06 million seven-year common stock purchase warrants were issued to the investors granting them the right to purchase our common stock at a price of $8.44 per share.

Table of Contents

Corporate information

Our corporate headquarters are located at 200 Connell Drive, Suite 1500, Berkeley Heights, NJ 07922, and our telephone number is (908) 517-7330, and this is where our medical and regulatory functions are also located. Our primary research facility is located in Dundee, Scotland. Dundee is the center of our structure-based drug design and development programs. A second research facility is located in Cambridge, England and is home to our Polgen division, which is focused on discovering the function of new cancer genes and validating their use as potential druggable targets.

Overview

We are a development-stage biopharmaceutical company dedicated to the discovery, development and eventual commercialization of novel, mechanism-targeted drugs to treat human cancers and other serious disorders. Our core area of expertise is in cell cycle biology, or the processes by which cells divide and multiply. We focus primarily on the discovery and development of orally available anticancer agents that target the cell cycle with the aim of slowing the progression or shrinking the size of tumors, and enhancing quality of life and improving survival rates of cancer patients. We have been focused on the cell cycle since our inception. We were founded in 1996 by Professor Sir David Lane, a recognized leader in the field of tumor suppressor biology who discovered the p53 protein, which operates as one of the body's own anticancer 'drugs' by inhibiting cell cycle targets. In 1999, we were joined by Professor David Glover, a recognized leader in the mechanism of mitosis or cell division who discovered, among other cell cycle targets, the mitotic kinases, Polo and Aurora, enzymes that act in the mitosis phase of the cell cycle. Our expertise in cell cycle biology is at the center of our business strategy.

We are generating several families of anticancer drugs that act on the cell cycle including cyclin dependent kinase (CDK) and Aurora kinase (AK) inhibitors. Although a number of pharmaceutical and biotechnology companies are currently attempting to develop CDK inhibitor drugs, we believe that our lead drug candidate, seliciclib, is the only orally available CDK inhibitor drug candidate currently in Phase II trials.

We have executed our strategy through the following activities:

Advancing our research and development programs

- June 2006, started sapacitabine Phase I trial in advanced leukemias
- June 2006, started seliciclib single agent randomized Phase IIb trial in non-small cell lung cancer
- November 2006, reported sapacitabine Phase I study results in solid tumors or lymphomas at the 18th NCI-EORTC-AACR symposium on 'Molecular Targets and Cancer Therapeutics'
- December 2006, reported sapacitabine interim Phase I data in advanced leukemias or myelodysplastic syndromes
- December 2006, CYC116 IND filed.

Strengthening our financial position

- March 2006, reverse merger with Xcyte provided Nasdaq a stock market listing and $21.6 million of cash and cash equivalents
- April 2006, raised net proceeds of $42.6 million through a private placement of equity
- Ended 2006 with approximately $54.0 million of cash
- February 2007, raised net proceeds of approximately $33.3 million through a registered direct offering

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Table of Contents

Enhancing our management team and board of directors

- October 2006, named John Womelsdorf, PhD., Vice President, Business Development
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March 9, 2007, appointed Pierre Legault as a non-executive director and chairman of the Audit Committee. Mr. Legault is currently Executive Vice President, The Jean Coutu Group (PJC) Inc. and President US, Brooks Eckerd.

We are advancing three of our anticancer drug candidates, seliciclib, sapacitabine and CYC116 through in-house research and development activities. We are also progressing further novel drug series, principally for cancer, which are at earlier stages. Taken together, our pipeline covers all four phases of the cell cycle, which we believe will improve the chances of successfully developing and commercializing novel drugs that work on their own or in combination with approved conventional chemotherapies or with other targeted drugs to treat human cancers.

Drug Candidate Pipeline

The table below summarizes our current clinical and preclinical programs.

Program	Indication	Development Status	Target	Cell Cycle Mechanism
Oncology Programs				
Seliciclib, (CYC202)	Non-small cell lung cancer	Phase IIb randomized trial on-going	CDK2/A, 2/E, 9	G1/S checkpoint and others
	Nasopharyngeal carcinoma	Phase I independent investigator study completed	CDK2/A, 2/E, 9	G1/S checkpoint and others
Sapacitabine, (CYC682)	Cancer	Phase Ib clinical trial in advanced leukemias on-going	DNA polymerase	G2 phase
CYC116	Cancer	IND filed December 2006	Aurora kinase & VEGFR2	Mitosis
CDK Inhibitors, Second Generation	Cancer	Preclinical	CDK	G1/S checkpoint and others
Clotrimazole Analogs	Cancer	Preclinical	Cyclin expression blocker	G1 phase
Plk Inhibitors	Cancer	Preclinical	Plk	G2/M checkpoint
Hdm2 Inhibitors	Cancer	Preclinical	Hdm2	G1 phase
Cyclin Binding Groove Inhibitors	Cancer	Preclinical	Cyclin binding groove	G1 phase
Other therapeutic areas				
Cell Cycle Inhibitors	Inflammatory Kidney Diseases	Preclinical (Phase I trials completed with seliciclib)	CDK	G1/S checkpoint and others
Cell Cycle Inhibitors	HIV/AIDS	Preclinical	CDK	Several
GSK-3 Inhibitors	Type 2 Diabetes	Preclinical	GSK-3	N/A

Market opportunity in oncology

Cancer remains a major life-threatening disease in the United States with approximately 3.2 million people afflicted by cancer and approximately 1.4 million new cases diagnosed every year. Five common

Table of Contents

cancer types: non-small cell lung, breast, ovarian, prostate and colorectal cancers, represent over 50% of all new cases of cancer in the United States each year and account for more than 50% of all cancer deaths in the United States. There are an estimated 172,570 patients diagnosed annually with lung cancer in the United States with another 381,500 new cases in the European Union. The prognosis for non-small cell lung cancer is poor with 5-year survival rates for patients standing at 15%.

Oncology development Programs

Seliciclib

Our lead drug candidate, seliciclib, is a novel, first-in-class, orally available, CDK inhibitor. The compound selectively inhibits multiple enzyme targets — CDK2/E, CDK2/A, CDK7 and CDK9 — that are central to the process of cell division and cell cycle control. Preclinical studies have shown that the drug works by inducing cell apoptosis, or cell suicide, in multiple phases of the cell cycle. To date, seliciclib has been evaluated in approximately 250 patients enrolled on several Phase I and II studies and has shown early signs of anti-cancer activity.

We have completed two Phase I trials that enrolled 24 healthy volunteers and three Phase I trials that enrolled a total of 84 cancer patients testing different doses and schedules. The primary toxicities observed were of a non-hematological nature including asthenia or weakness, elevation of liver enzymes, hypokalemia or decreased potassium levels, nausea and vomiting and elevation in creatinine. Although these trials were designed to test safety rather than efficacy of seliciclib given alone as monotherapy in patients with solid tumors who failed multiple previous treatments, several of these patients appeared to have benefited from seliciclib treatment.

Seliciclib was shown in a further Phase I study sponsored and conducted by independent investigators to have clinical antitumor activity in patients with nasopharyngeal cancer, measured as a decrease in the size of primary tumor and clinically abnormal lymph nodes, as well as evidence of tumor cell deaths by biomarker analyses. Four Phase II trials have been conducted in cancer patients to evaluate the tolerability and antitumor activities of seliciclib alone or in combination with standard chemotherapies used in the treatment of advanced non-small cell lung cancer or breast cancer. Interim data from two Phase II open label studies of a total of 52 patients with non-small cell lung cancer suggest that seliciclib treatment did not aggravate the known toxicities of standard first and second-line chemotherapies nor appear to cause unexpected toxicities, although these trials were not designed to provide statistically significant comparisons. The combination of seliciclib with standard dose of capecitabine was not well tolerated in patients with advanced breast cancer. The Phase II trial of seliciclib as monotherapy for the treatment of hematological cancers has been closed. We expect to report final data within the first half of 2007.

Based on our observations of tolerability and antitumor activity of seliciclib in the clinical trials conducted to date, the oral availability of seliciclib, the recommendation of a non-small cell lung cancer expert panel, and regulatory and marketing considerations, seliciclib is currently being evaluated in the APPRAISE trial, a Phase IIb randomized double-blinded study to evaluate the efficacy and safety of the drug as a third line treatment in patients with NSCLC. The trial, which is expected to enroll approximately 200 patients, is using a randomized discontinuation trial design. We expect to report data in the fourth quarter of 2007. Additionally, based on the results observed by independent

investigators on clinical antitumor activity in patients with nasopharyngeal cancer we plan to commence a randomized Phase II trial in nasopharyngeal carcinoma in the second half of 2007. We have retained the worldwide rights to commercialize seliciclib.

Sapacitabine

Our second drug candidate, sapacitabine, is an orally available prodrug of CNDAC, which is a novel nucleoside analog, or a compound with a structure similar to a nucleoside. A prodrug is a compound that has a therapeutic effect after it is metabolized within the body. CNDAC has a significantly longer residence time in the blood when it is produced in the body through metabolism of sapacitabine than when it is given directly. Sapacitabine acts through a dual mechanism whereby the compound interferes

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Table of Contents

with DNA synthesis by causing single-strand DNA breaks and induces arrest of the cell division cycle at G2 phase. A number of nucleoside drugs, such as gemcitabine, or Gemzar®; Eli Lilly and cytarabine (Ara-C), are in wide use as conventional chemotherapies. Both sapacitabine and its major metabolite, CNDAC, have demonstrated potent anti-tumor activity in both blood and solid tumors in preclinical studies. In a liver metastatic mouse model, sapacitabine was shown to be superior to gemcitabine or 5-FU, two widely used nucleoside analogs, in delaying the onset and growth of liver metastasis.

Two Phase I studies of sapacitabine have been completed in the United States by Sankyo, from which we in-licensed sapacitabine, evaluating 87 patients in refractory solid tumors. A Phase Ib dose escalation clinical trial is currently in progress in the United States for the treatment of patients with refractory solid tumors or lymphomas. Preliminary results from this study were reported at the meeting of the 18th EORTC-NCI-AACR Molecular Targets and Cancer Therapeutics in November 2006. The primary objective of the study was to evaluate the safety profile of sapacitabine administered twice daily for 14 consecutive days or 7 consecutive days every 21 days. Of the 37 treated patients, 28 received the drug twice daily for 14 days and 9 received the drug twice daily for 7 days. The dose-limiting toxicity was reversible myelosuppression. One patient treated at the maximum tolerated dose died of candida sepsis in the setting of grade 4 neutropenia and thrombocytopenia. Non-hematological toxicities were mostly mild to moderate. The best response by investigator assessment was stable disease in 13 patients, five with non-small cell lung cancer, two with breast cancer, two with ovarian cancer and one each with colorectal cancer, adenocarcinoma of unknown primary, gastrointestinal stroma tumor, and parotid acinar carcinoma. The primary toxicity was reversible myelosuppression.

Sapacitabine is also currently being evaluated in a Phase I clinical trial in advanced leukemias and myelodysplastic syndromes, or MDS. The Phase I study is being conducted by Dr. Hagop Kantarjian, Professor of Medicine and Chairman of the Leukemia Department at M.D. Anderson Cancer Center in Houston, Texas. The study's primary objective is to determine the maximum tolerated dose (MTD) of sapacitabine administered twice daily, or b.i.d., by mouth for seven consecutive days every 21 days. As of November 2006, preliminary interim data was available on 22 patients, of which nine had de novo acute myelogenous leukemia, or AML; seven had AML preceded by MDS; three had MDS-refractory anemia with excess blasts, or MDS-RAEB; and one each had treatment-related AML, acute lymphocytic leukemia, or ALL and chronic lymphocytic leukemia or CLL. Twenty-one patients received prior chemotherapy and one elderly patient (aged 91) did not receive any prior chemotherapy. The median number of prior chemotherapy regimens is two, ranging from one to four. Fifteen patients were previously treated with Ara-C-containing regimens of which nine had de novo AML and six had AML preceded by MDS. Six patients were

previously treated with decitabine of which three had MDS-RAEB, one had de novo AML, one had AML preceded by MDS and treatment-related AML. One patient treated at the dose level of 275 mg b.i.d. experienced a dose limiting toxicity, or DLT consisting of Grade 3 diarrhea and Grade 3 neutropenic colitis, which resolved after cessation of dosing and medical treatment. No DLTs were reported in the remaining five patients treated at 275 mg b.i.d. Dose escalation continues and the MTD has not been reached at the dose level of 325 mg b.i.d., which is approximately four times the recommended Phase II dose for solid tumor patients. To date, the best response to sapacitabine was reduction in bone marrow blast counts to 5% or less, which was observed in seven patients of which three had de novo AML, two had AML preceded by MDS, and two had MDS-RAEB.

We plan to start Phase II evaluation of sapacitabine both in solid tumors and hematological malignancies in the second half of 2007. We have retained worldwide rights to commercialize sapacitabine with the exception of Japan where Sankyo has a right of first refusal to market the drug under terms to be negotiated.

CYC116

We have selected CYC116 as a lead development candidate from our Aurora kinase inhibitor program. In this program, several compounds have demonstrated efficacy by oral administration in hematological and solid tumor models with a mechanism consistent with inhibition of the target. We submitted in December 2006 an Investigational New Drug, or IND application, with the Food and Drug Administration, or FDA, to begin clinical trials of CYC116, an orally-active inhibitor of Aurora kinases A & B and VEGFR2, for the treatment of cancer. Aurora kinases are a family of serine/threonine protein

Table of Contents

kinases that are only expressed in actively dividing cells and are crucial for the process of cell division, or mitosis. These proteins, which have been found to be over-expressed in many types of cancer, have generated significant scientific and commercial interest as cancer drug targets. Aurora kinases were discovered by Professor David Glover, Chief Scientist of our Polgen Division. VEGFR2 is a receptor protein that is part of an important and validated pathway in angiogenesis, or blood vessel formation. We have retained worldwide rights to commercialize CYC116.

In our development programs, we have been an early adopter in the use of biomarker analysis to help evaluate whether our drug candidates are having their intended effect through their assumed mechanisms. Biomarkers are proteins or other substances whose presence in the blood can serve as an indicator or marker of diseases. Biomarker data from early clinical trials may also enable us to design subsequent trials more efficiently and to monitor patient compliance with trial protocols. We believe that in the longer term biomarkers may allow the selection of patients more likely to respond to its drugs for clinical trial and marketing purposes and increase the benefit to patients.

Other Oncology Programs

Second Generation CDK Inhibitors

We have discovered over 600 novel CDK inhibitors that are members of a different chemical family than seliciclib. Based on their observed properties in preclinical tests, we believe that these second-generation compounds may prove to be even more potent anticancer agents than seliciclib.

Clotrimazole Analogs

We have licensed from Lorus Therapeutics, Inc. a group of compounds based on CYC381, an orally available analog of clotrimazole, a commonly used antifungal drug. Investigators at Harvard Medical School observed that clotrimazole analogs exhibit anticancer activity by inhibiting internal calcium channels in cells and blocking the expression of important cell cycle targets called cyclins. Extensive preclinical testing prior to our licensing CYC381 suggested that it may be active in slowing the progression of several solid tumors in vivo. CYC381 is a racemic mixture or a combination of two different chemicals, called enantiomers, which cannot be easily separated. Before progressing into further development we must reproduce evidence of anticancer activity by one or more enantiomers with that reported by others before we in-licensed CYC381.

Plk Inhibitors

Our Polo-like kinase, or Plk, inhibitor program targets the mitotic phase of the cell cycle with the objective of identifying potent and selective compounds which inhibit Plk1, a kinase active during mitosis. Inhibition of Plk1 results in cell cycle arrest at the G2/M checkpoint and induces apoptosis in cancer cells. Our Plk inhibitor program represents the first target gene that has emerged through the target validation process at our Polgen division and progressed to the drug discovery and chemistry stage. Because little was known about the nature and structure of Plk1, and because Plk to our knowledge has never been crystallized, we relied on advanced computer modeling and software-based design techniques to identify a series of compounds which selectively inhibit Plk.

Hdm2 Inhibitors

One of the key cell cycle regulatory proteins is p53. When active, p53 causes cell arrest at the G1/S checkpoint, inducing apoptosis in cancer cells. Under normal circumstances, p53 is held in an inactive form by binding to another regulatory protein, Hdm2. In this program, we have investigated ways of disrupting the interaction between Hdm2 and p53, thus activating p53. Through virtual screening technologies, we have identified two small molecule groups capable of breaking the binding between p53 and Hdm2.

Cyclin Binding Groove Inhibitors

The activity of CDK can be inhibited by two methods, either by blocking the ATP site, as is the case with seliciclib, or by inhibiting the substrate binding site on the cyclin protein. Preventing the cyclin from

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Table of Contents

binding results in cell cycle arrest and induces apoptosis in cancer cells. We are currently investigating the development of such cyclin binding groove inhibitors, continuing a program that was the subject of a two-year collaboration with AstraZeneca that concluded in mid-2003. We retain all of the intellectual property associated with this program upon its conclusion.

Non-oncology Programs

Cell Cycle Inhibitors in Inflammatory Kidney Disease

Preclinical results from several independent investigators suggest that cell cycle inhibitors such as seliciclib may also have a therapeutic benefit in the treatment of patients with inflammatory kidney diseases, which are sometimes referred to as glomerulonephritis. Because seliciclib acts to arrest the progress of the cell cycle, we believe it may be

particularly effective in treating those forms of glomerulonephritis characterized by excessive cell proliferation. The most common forms of these are IgA nephritis and lupus nephritis.

We entered into an evaluation and option agreement with Genzyme Corporation under which Genzyme evaluated two preclinical stage CDK inhibitors for development as drugs for renal disease. We will be terminating the arrangement, although Genzyme may continue to have certain so called first negotiation rights for a period of time.

CDK Inhibitors in Virology

Cell cycle inhibitors may be useful in the treatment of viral diseases to the extent that drugs can be developed that prevent the replication of virus-infected host cells and cause their death by apoptosis while sparing most uninfected cells. If this is proven in humans, cell cycle inhibitors may have significant potential in this area, as they do not interfere with viruses and are less likely to induce viral resistance, a major cause of failure in antiviral drugs that attack the virus itself. We have investigated a number of compounds in this program, some of which appear to be highly active against HIV in biological tests and induce antiviral effects that may be as or more potent than many existing HIV/AIDS therapeutic agents. We intend to progress this program through collaboration with groups who specialize in anti-viral research.

GSK-3 Inhibitors in Type 2 Diabetes

Glycogen Synthase Kinase-3, or GSK-3, inhibition is an essential element in the body’s regulation of blood sugar. GSK-3 regulates the glycogen synthase enzyme that indirectly controls glucose levels. Insulin controls the regulation of energy conversion and storage by interacting with its receptor which results in the activation of PI-3 kinase that in turn inhibits GSK-3. In adult onset or Type 2 Diabetes, GSK-3 is not inhibited because the insulin receptor is not operating properly. As a result, we believe that GSK-3 inhibitor drugs may be suitable for development as Type 2 Diabetes therapies. The structures of GSK-3 and CDK are very similar. In our cancer programs, it was desirable to discover highly specific CDK inhibitors that do not inhibit GSK-3. Our work in this area prompted the investigation of highly specific GSK-3 inhibitors that do not inhibit CDK. We have identified four chemical families of GSK-3 inhibitors some of which are potent at picomolar concentrations, representing the most potent GSK-3 inhibitor compounds disclosed in the literature. We have selected two lead compounds from this series, both of which have achieved proof-of-concept in a standard model of diabetes, demonstrating stimulation of glycogen synthase, improvement in glucose tolerance and regulation of triglycerides. We intend to progress this program through collaboration with groups who are specialized in diabetes research.

Technology and expertise

Our approach to drug discovery and development relies on proprietary genomic technology to identify gene targets, which are then progressed by means of structure-based design techniques through to the development stage. This approach is exemplified by our Aurora kinase and Plk, or Polo-like kinase, inhibitor programs. Fundamentally, this approach to drug discovery and design aims to improve our

Table of Contents

ability to select promising drug targets in the early stages of the process so as to decrease compound attrition rates during the later, more expensive stages of drug development. We devote more resources initially to enrich the target selection process, so that we focus our efforts on targets that have a higher probability of yielding successful drug

candidates. To this end, we have assembled an integrated suite of sophisticated discovery and design technologies, together with highly skilled personnel.

Business Strategy

Focus on the cell cycle and cancer

We are and intend to remain strongly focused on the development of novel, cell cycle-based therapies for the treatment of cancer and other serious disease indications, for a number of reasons:

- Our core area of expertise is in cell cycle biology and our scientists include recognized leaders in this field. In addition, our senior management has extensive experience in research, preclinical and clinical development, sales and marketing. Thus, we believe that we are well placed to exploit the significant opportunities that this area offers for new drug discovery and development.
- The novel, mechanism-targeted cell cycle drugs we are developing are designed to be highly selective in comparison to conventional chemotherapies, potentially inducing death in cancer cells while sparing most normal cells which may give rise to fewer side-effects.
- We believe that we are the only company with an orally available CDK inhibitor drug candidate in Phase II clinical trials and that, with a deep pipeline of other anticancer drug candidates in clinical or preclinical development, we believe we are currently well positioned to realize some of the market potential of such drugs.

Develop anticancer drug candidates in all phases of the cell cycle and multiple compounds for particular cell cycle targets

Targeting a broad development program focused on multiple phases of the cell cycle allows us to minimize risk while maximizing the potential for success and also to develop products that are complementary to one another.

Enter into partnering arrangements selectively, while developing our own sales and marketing capability

We retain all marketing rights to the compounds associated with the current clinical-stage drug programs. To optimize our commercial return, we intend to both enter into selected partnering arrangements, and to develop our sales and marketing capability initially by retaining co-promotion rights. Generally we develop compounds through the Phase II proof-of-efficacy stage before seeking a partner. We may be prepared to enter into partnering arrangements earlier in connection with drug programs outside the current anticancer core competency.

Patents, Proprietary Technology and Collaborations

We consider intellectual property rights to be vital and use a variety of methods to secure, protect and evaluate these rights. These include:

- Ownership and enforcement of patent rights
- Patent applications covering our own inventions in fields that we consider important to its business strategy
- License agreements with third parties granting us rights to patents in fields that are important to its business strategy
- Invention assignment agreements with our employees and consultants
- Non-compete agreements with our employees and consultants
- Confidentiality agreements with our employees, consultants, and others having access to its proprietary information

Table of Contents

- Standard policies for the maintenance of laboratory notebooks to establish priority of our inventions
- Freedom to use studies from patent counsel
- Material transfer agreements
- Trademark protection

In addition to its 22 U.S. patents, we own 10 patents that were granted by the European Patent Office, or EPO, for designated European countries, and 15 issued patents in other countries. The European granted patents expire between 2015 and 2022. In addition to the licenses we hold in 21 patents issued in the United States, we hold licenses under 75 issued patents worldwide, 16 granted by the EPO for designated European countries and 59 issued in other countries. The licensed European granted patents expire between 2011 and 2022. Our patent strategy is to file patents on compounds and technologies in countries and jurisdictions that it considers important to its business. We usually files first in the United Kingdom and then extend our applications to other countries through the Patent Cooperation Treaty. In some cases, we file directly in the United States. We give priority to obtaining substance of matter claims in the United States, the European Patent Office, Japan and other important countries if such protection is available. We prefer substance of matter claims because they give us rights in our compounds themselves, and not merely in a particular use of the compounds. In addition to substance of matter claims, we seek coverage for medical uses, combination therapies, pharmaceutical forms of our compounds and synthetic routes where available and appropriate. Claims covering combination therapies and pharmaceutical forms can be valuable because the therapeutic effect of pharmaceuticals used in the anticancer field is often enhanced when individual therapeutics are used in particular combinations. The availability of protection in these areas can, however, vary from jurisdiction to jurisdiction and combination claims are particularly difficult to obtain for many inventions. We own 44 patent applications pending in the United States, 38 before the European Patent Office, 8 pending PCT applications still in the international application phase, and over one hundred pending patent applications in other countries. Ten of this last group of pending patent applications were first filed, and have an earliest priority date, within the last twelve months. No assurances can be given that patents will be issued with respect to the pending applications, nor that the claims will provide equivalent coverage in all jurisdictions. Under the terms of our agreements with several universities and research institutions we also have the right to apply for patents in the name of those universities and institutions for inventions in which license rights are held. This gives us the ability to control the prosecution of patents that directly relate to business strategy. In addition to the pending patent applications referred to above that we own, there are 54 pending patent applications worldwide to which we have a license or an option to take a license.

Our patent filings for the second-generation CDK inhibitor research program exemplify our patent strategy. Out of over 600 compounds under investigation in this program we have filed patent applications seeking substance of matter protection that may be roughly grouped into 12 patent families. Of these, we have made a European application designating all European Patent Convention member states and direct national filings in the United States, Japan and several additional countries covering the compounds that we believe to be the most promising from a commercial standpoint. We have made additional Patent Cooperation Treaty filings covering derivative compounds, medical uses and related technology. The first patent application from the family of compound patents has resulted in the issuance of two U.S. patents with substance of matter claims covering a specific genus of compounds showing activity in its preclinical and research programs. Although issuance of a substance of matter claim in the United States is an indication that other countries may grant similar protection, the pending applications may not result in additional patent protection.

We hold patents to several technology-based systems, including families of patents covering its Fluorescience fluorescent assay techniques and the drug delivery system Penetratin. We have filed a portfolio of patents claiming the use of over one hundred specific genes as drug targets based on the identification of their function in mitosis.

Since publications in the scientific or patent literature often lag behind actual discoveries, we are not certain of being first to make the inventions covered by each of its pending patent applications or the first

Table of Contents

to file those patent applications. Generally, patent applications in the United States are maintained in secrecy for a period of 18 months or more, which increases the uncertainty we face. Moreover, the patent positions of biotechnology and pharmaceutical companies are highly uncertain and involve complex legal and factual questions. As a result, we cannot predict the breadth of claims allowed in biotechnology and pharmaceutical patents, or their enforceability. To date, there has been no consistent policy regarding the breadth of claims allowed in biotechnology patents. Third parties or competitors may challenge or circumvent our patents or patent applications, if issued. Because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that before we commercialize any of its products, any related patent may expire, or remain in existence for only a short period following commercialization, thus reducing any advantage of the patent and the commercial opportunity of the product.

If patents are issued to others containing valid claims that cover our compounds or their manufacture or use or screening assays related thereto, we may be required to obtain licenses to these patents or to develop or obtain alternative technology. We are aware of several pending patent applications, and understands that others may exist, that could support claims that, if granted, would cover various aspects of its developmental programs, including in some cases particular uses of its lead drug candidate, seliciclib, sapacitabine or other therapeutic candidates, or gene sequences and techniques that we use in the course of its research and development. In addition, we understand that other applications exist relating to uses of seliciclib and sapacitabine that are not part of its current clinical programs for those compounds. Although we intend to continue to monitor these applications, it is not possible to predict whether these claims will ultimately be allowed or if they were allowed what their breadth would be. In addition, we may need to commence litigation to enforce any patents issued to us or to determine the scope and validity of third-party proprietary rights. Litigation would create substantial costs. In one case we have opposed a granted European patent relatetd to human aurora kinase. We are also aware of a corresponding US patent containing method of treatment claims for specific cancers using aurora kinase modulators, which if held valid, could potentially restrict the use of certain of our aurora kinase inhibitors. If competitors prepare and file patent applications in the United States that claim technology that we also claim, we may have to participate in interference proceedings in the U.S. Patent and Trademark Office to determine which invention has priority. These proceedings could result in substantial costs, even if the eventual outcome is favorable to us. An adverse outcome in litigation could subject us to significant liabilities to third parties and require it to seek licenses of the disputed rights from third parties or to cease using the technology, even a therapeutic product, if such licenses are unavailable or too expensive.

Licenses

Several of our programs are based on technology licensed from others. Our breach of an existing license or failure to obtain a license to technology required to develop, test and commercialize our products may seriously harm our business.

Seliciclib

We have entered into an agreement with Centre National de Recherche Scientifique, or CNRS, and Institut Curie that grants it worldwide rights under the patents jointly owned by CNRS, Institut Curie and the Czech Institute of Experimental Botany covering the seliciclib compound. The effective date of the agreement is February 1, 2002. The license grants exclusive rights in the fields of auto-immune diseases, cardiovascular diseases, dermatological diseases, infectious diseases, inflammatory diseases, and proliferative diseases, including cancer. Non-acute chronic diseases of the central nervous system, neurological diseases and diseases of the peripheral nervous system are specifically excluded. The license runs for the term of the patents in each country, or for ten years from the first commercial sale in each country, whichever is later. Under the agreement, we paid an up-front fee. We also made yearly payments and milestone payments until the patents covering the seliciclib compound, particular uses of the compound, and particular derivatives of the compound were published as granted in either the United States or by the European Patent Office which took place in 2001 and 2003, respectively. Milestones are also paid on the first commercialization of a product that consists of a new chemical entity that is covered by one of the licensed patents. We pay royalties based on our net sales of products covered by the patents.

Table of Contents

Royalties are payable on a country-by-country basis for the term of patent protection in each country or ten years from the first commercial sale of royalty-bearing products in that country, whichever is later. Royalties are payable on net sales. Net sales are defined as the gross amount invoiced by us or by our affiliates for the products, less normal trade discounts, credits for returned products, taxes and shipping charges. There is one royalty rate for products that are covered by valid licensed patent claims and a second, lower royalty rate for all other products that require a license under the licensed patents. The royalties payable under the agreement are reduced if we are required to pay royalties with respect to patents other than the ones licensed under this agreement and the total amount of royalties that we are required to pay exceeds a fixed percentage amount. The amount of reduction depends on the amount by which our total royalties exceed the fixed amount. We must also pay a portion of sublicensing revenues. The portion of sublicensing revenues that we are required to pay is reduced if we have taken the sublicensed product into human clinical trials. Although the license permits us to grant sublicenses, we cannot assign the license without the consent of the CNRS and Institut Curie, which may not be unreasonably withheld. Under the agreement, assignment is defined to include many transactions of the type that we might wish to pursue, such as a merger or an acquisition by another company, as well as certain takeovers. This restriction may prevent us from pursuing attractive business opportunities. Moreover, the occurrence of a majority takeover or a similar transaction that we may be unable to control could cause a default under the license agreement, which could lead to its termination.

We have also purchased from the Czech Institute of Experimental Botany patents and patent applications covering the use of seliciclib and related compounds. The issued patents are in the United States and Australia. Under the purchase agreement, we will pay royalties to the Czech Institute upon sales of products covered by those patents, but only if there are no royalties paid by us to CNRS for those sales under the license agreement with CNRS and Institut Curie covering seliciclib that is described above.

Patents covering the seliciclib compound are owned jointly by the Czech Institute and CNRS. The patents have been issued in the United States and by the European Patent Office and expire in 2016. It may be possible to extend the term of a patent in the United States or Europe for up to five years to the extent it covers the seliciclib compound upon regulatory approval of that compound in the United States or Europe, but there is no assurance that we will be able to obtain any such extension. Under agreements between CNRS and the Czech Institute, CNRS has the exclusive right to

enter into license agreements covering the patents. The agreement reserves to both CNRS and the Czech Institute certain rights, including the right to patent improvements and to use the patents for internal research purposes.

Sapacitabine

We have entered into a license agreement with Sankyo Co., Ltd. of Japan with respect to patents and patent applications covering the sapacitabine compound and patent applications claiming polymorphic forms of sapacitabine and methods for its preparation and use as well as related know-how and materials. The agreement has a commencement date of September 10, 2003. The issued patents for the sapacitabine compound cover the United States, the European Patent Office, Japan and 20 other countries. These patents expire between 2012 and 2014. It may be possible to extend the term of a patent in the United States or Europe for up to five years to the extent it covers the sapacitabine compound upon regulatory approval of that compound in the United States or Europe, but there is no assurance that we will be able to obtain any such extension. The license grants us the exclusive right to exploit and sublicense the sapacitabine compound and any other products covered by the patents and patent applications owned by Sankyo. The license originally was subject to certain third party rights related to certain countries but the license has been extended and is now worldwide. The license agreement also grants us nonexclusive, sublicensed rights in CNDAC, both the precursor compound and initial metabolite of sapacitabine. We are under an obligation to use reasonable endeavors to develop a product and we have agreed to pay Sankyo an up-front fee, reimbursement for Sankyo's enumerated expenses, milestone payments and royalties on a country-by-country basis. Under this agreement, aggregate milestone payments totaling $11.7 million could be payable subject to achievement of all the specific contractual milestones and our decision to continue with these projects. The up-front fee and certain past reimbursement have been paid. Royalties are payable in each country for the term of patent protection in the country or for ten years

Table of Contents

following the first commercial sale of licensed products in the country, whichever is later. Royalties are payable on the net sales. Net sales are defined as the gross amount invoiced by us or our affiliates or licensees, less discounts, credits, taxes, shipping and bad debt losses. The agreement extends from its commencement date to the date on which no further amounts are owing under it. If we wish to appoint a third party to develop or commercialize a sapacitabine-based product in Japan, within certain limitations, Sankyo must be notified and given a right of first refusal to develop and/or commercialize in Japan. In general, the license may be terminated by us for technical, scientific, efficacy, safety, or commercial reasons on six months notice (twelve if after launch of sapacitabine-based product) or by either party for material default. On termination, if Sankyo wishes to acquire an exclusive license to sapacitabine intellectual property developed by us during the term of the license, Sankyo may notify us and the parties will meet to negotiate commercial terms in good faith. If agreement cannot be reached, the terms of the exclusive license are to be determined by an expert.

Clotrimazole Analogs and CYC381

We have entered into a license agreement with NuChem Pharmaceuticals, Inc. and its parent Lorus Therapeutics, Inc. with respect to our license of patents and patent applications covering the CYC381 compound in the United States, the European Patent Office, Japan and other countries, as well as related know-how, materials and technology. The effective date of the agreement is September 22, 2003. Patents containing substance of matter claims covering the compound have been issued in the United States, Australia, New Zealand, Singapore and China. These patents and patent applications if and when granted will expire in 2017 and 2018. It may be possible to extend the term of a patent

in the U.S. or Europe for up to five years to the extent it covers the CYC381 compound upon regulatory approval of that compound in the U.S. or Europe, but there is no assurance that we will obtain any such extension.

The license grants us worldwide rights in the technology owned by and licensed to NuChem related to a class of compounds including CYC381 and two other chemical classes of compounds that might have similar effects. The license is limited to the diagnosis and treatment of cancer (including leukemias), Kaposi's sarcoma and actinic keratosis. To the extent that the patents and related technology are owned by or exclusively licensed to NuChem, the license is exclusive. It is nonexclusive for patents and technology that are nonexclusively licensed to NuChem. We have the right to sublicense these patents and technology to others. Improvements to the licensed patents are owned by NuChem and licensed back to us. On termination, NuChem may obtain, on commercially reasonable terms, a license of the results of the research and development that we perform on CYC381. We are responsible for prosecution, maintenance and defense of the licensed patents, including all associated costs. NuChem co-owns certain of the patents with Harvard University and Ion Pharmaceuticals and Harvard University retains certain rights to use the patents for research purposes. No warranty is given under the agreement as to the validity of the licensed patents or that 'any of the NuChem IP can be practiced or exploited without infringing other patents.' We are obligated to use commercially reasonable efforts to develop and commercialize the patents. The agreement extends from its commencement date to the date on which no further amounts are owing under it. The agreement may be terminated by us for convenience after September 2004 on four months' notice, by either party if the other defaults, and by NuChem if we do not actively pursue the licensed technology. We paid NuChem an up-front fee. We agreed to make milestone and royalty payments on a country-by-country basis and to pay NuChem a portion of any sublicensing fees it receives.

We have entered into a license agreement with Johnson Matthey Pharmaceutical Materials, Inc. with respect to U.S. and European Patent Office patents as well as patent applications pending in Japan and certain other jurisdictions that claim the synthetic route for CYC381. The effective date of the agreement is September 1, 2003. These patents and applications if and when granted will expire between 2017 and 2018. The license grants us the exclusive worldwide right to manufacture and sell products under the Johnson Matthey patents. The license includes the right to sublicense. We paid an up-front fee and agreed to make minimum annual payments, including with respect to each sublicense and to pay a royalty on the net cost of goods manufactured under the license. We also agreed to give Johnson Matthey the right to bid for any contract to manufacture products under the license. The license runs for the term of the patents. We may terminate the license for convenience, and either party may terminate it for the default of the other.

Table of Contents

Government Regulation

The U.S. Food and Drug Administration, or FDA, and comparable regulatory agencies in state and local jurisdictions and in foreign countries impose substantial requirements upon the clinical development, manufacture, marketing and distribution of drugs. These agencies and other federal, state and local entities regulate research and development activities and the testing, manufacture, quality control, safety, effectiveness, labeling, storage, record keeping, approval, advertising and promotion of our drug candidates and drugs.

In the United States, the FDA regulates drugs under the Federal Food, Drug and Cosmetic Act and implementing regulations. The process required by the FDA before our drug candidates may be marketed in the United States generally involves the following:

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completion of extensive preclinical laboratory tests, preclinical animal studies and formulation studies, all performed in accordance with the FDA's good laboratory practice, or GLP, regulations;

- submission to the FDA of an IND application which must become effective before clinical trials may begin;
- performance of adequate and well-controlled clinical trials to establish the safety and efficacy of the drug candidate for each proposed indication;
- submission of a new drug application, or NDA, to the FDA;
- satisfactory completion of an FDA preapproval inspection of the manufacturing facilities at which the product is produced to assess compliance with current GMP, or cGMP, regulations; and
- FDA review and approval of the NDA prior to any commercial marketing, sale or shipment of the drug.

This testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for our drug candidates will be granted on a timely basis, if at all. Preclinical tests include laboratory evaluation of product chemistry, formulation and stability, as well as studies to evaluate toxicity in animals. The results of preclinical tests, together with manufacturing information and analytical data, are submitted as part of an IND application to the FDA. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions about the conduct of the clinical trial, including concerns that human research subjects will be exposed to unreasonable health risks. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Our submission of an IND, or those of our collaborators, may not result in FDA authorization to commence a clinical trial. A separate submission to an existing IND must also be made for each successive clinical trial conducted during product development. Further, an independent institutional review board, or IRB, for each medical center proposing to conduct the clinical trial must review and approve the plan for any clinical trial before it commences at that center and it must monitor the clinical trial until completed. The FDA, the IRB or the clinical trial sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk. Clinical testing also must satisfy extensive Good Clinical Practice, or GCP, regulations and regulations for informed consent.

Clinical Trials: For purposes of an NDA submission and approval, clinical trials are typically conducted in the following three sequential phases, which may overlap:

- Phase I: The clinical trials are initially conducted in a limited population to test the drug candidate for safety, dose tolerance, absorption, metabolism, distribution and excretion in healthy humans or, on occasion, in patients, such as cancer patients. Phase I clinical trial typically designed to evaluate the impact of the drug candidate in combination with currently approved drugs.

- Phase II: These clinical trials are generally conducted in a limited patient population to identify possible adverse effects and safety risks, to determine the efficacy of the drug candidate for specific targeted indications and to determine dose tolerance and optimal dosage. Multiple Phase II clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more expensive Phase III clinical trial.
- Phase III: These clinical trials are commonly referred to as pivotal clinical trials. If the Phase II clinical trials demonstrate that a dose range of the drug candidate is effective and has

an acceptable safety profile, Phase III clinical trials are then undertaken in large patient populations to further evaluate dosage, to provide substantial evidence of clinical efficacy and to further test for safety in an expanded and diverse patient population at multiple, geographically dispersed clinical trial sites.

In some cases, the FDA may condition approval of an NDA for a drug candidate on the sponsor's agreement to conduct additional clinical trials to further assess the drug's safety and effectiveness after NDA approval. Such post-approval trials are typically referred to as Phase IV clinical trials.

New Drug Application. The results of drug candidate development, preclinical testing and clinical trials are submitted to the FDA as part of an NDA. The NDA also must contain extensive manufacturing information. Once the submission has been accepted for filing, by law the FDA has 180 days to review the application and respond to the applicant. The review process is often significantly extended by FDA requests for additional information or clarification. The FDA may refer the NDA to an advisory committee for review, evaluation and recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. The FDA may deny approval of an NDA if the applicable regulatory criteria are not satisfied, or it may require additional clinical data or an additional pivotal Phase III clinical trial. Even if such data are submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data from clinical trials are not always conclusive and the FDA may interpret data differently than we or our collaborators do. Once issued, the FDA may withdraw a drug approval if ongoing regulatory requirements are not met or if safety problems occur after the drug reaches the market. In addition, the FDA may require further testing, including Phase IV clinical trials, and surveillance programs to monitor the effect of approved drugs which have been commercialized. The FDA has the power to prevent or limit further marketing of a drug based on the results of these post-marketing programs. Drugs may be marketed only for the approved indications and in accordance with the provisions of the approved label. Further, if there are any modifications to a drug, including changes in indications, labeling or manufacturing processes or facilities, we may be required to submit and obtain FDA approval of a new NDA or NDA supplement, which may require us to develop additional data or conduct additional preclinical studies and clinical trials.

Fast Track Designation. The FDA's fast track program is intended to facilitate the development and to expedite the review of drugs that are intended for the treatment of a serious or life-threatening condition for which there is no effective treatment and which demonstrate the potential to address unmet medical needs for the condition. Under the fast track program, the sponsor of a new drug candidate may request the FDA to designate the drug candidate for a specific indication as a fast track drug concurrent with or after the filing of the IND for the drug candidate. The FDA must determine if the drug candidate qualifies for fast track designation within 60 days of receipt of the sponsor's request.

If fast track designation is obtained, the FDA may initiate review of sections of an NDA before the application is complete. This rolling review is available if the applicant provides and the FDA approves a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, the time period specified in the Prescription Drug User Fees Act, which governs the time period goals the FDA has committed to reviewing an application, does not begin until the complete application is submitted. Additionally, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

In some cases, a fast track designated drug candidate may also qualify for one or more of the following programs:

- Priority Review. Under FDA policies, a drug candidate is eligible for priority review, or review within a six-month time frame from the time a complete NDA is accepted for filing, if the drug candidate provides a significant improvement compared to marketed drugs in the treatment, diagnosis or prevention of a disease. We cannot guarantee any of our drug candidates will receive a priority review designation, or if a priority designation is received, that review or approval will be faster than conventional FDA procedures, or that FDA will ultimately grant drug approval.
- Accelerated Approval. Under the FDA's accelerated approval regulations, the FDA is authorized to approve drug candidates that have been studied for their safety and effectiveness in treating serious or life-threatening illnesses, and that provide meaningful therapeutic benefit to patients over existing treatments based upon either a surrogate endpoint that is reasonably likely to predict clinical benefit or on the basis of an effect on a clinical endpoint other than patient survival. In clinical trials, surrogate endpoints are alternative measurements of the symptoms of a disease or condition that are substituted for measurements of observable clinical symptoms. A drug candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase IV or post-approval clinical trials to validate the surrogate endpoint or confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or to validate a surrogate endpoint or confirm a clinical benefit during post-marketing studies, will allow the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

When appropriate, we and our collaborators intend to seek fast track designation or accelerated approval for our drug candidates. We cannot predict whether any of our drug candidates will obtain a fast track or accelerated approval designation, or the ultimate impact, if any, of the fast track or the accelerated approval process on the timing or likelihood of FDA approval of any of our drug candidates.

Satisfaction of FDA regulations and requirements or similar requirements of state, local and foreign regulatory agencies typically takes several years and the actual time required may vary substantially based upon the type, complexity and novelty of the product or disease. Typically, if a drug candidate is intended to treat a chronic disease, as is the case with some of our drug candidates, safety and efficacy data must be gathered over an extended period of time. Government regulation may delay or prevent marketing of drug candidates for a considerable period of time and impose costly procedures upon our activities. The FDA or any other regulatory agency may not grant approvals for new indications for our drug candidates on a timely basis, if at all. Even if a drug candidate receives regulatory approval, the approval may be significantly limited to specific disease states, patient populations and dosages. Further, even after regulatory approval is obtained, later discovery of previously unknown problems with a drug may result in restrictions on the drug or even complete withdrawal of the drug from the market. Delays in obtaining, or failures to obtain, regulatory approvals for any of our drug candidates would harm our business. In addition, we cannot predict what adverse governmental regulations may arise from future United States or foreign governmental action.

Other regulatory requirements. Any drugs manufactured or distributed by us or our collaborators pursuant to FDA approvals are subject to continuing regulation by the FDA, including recordkeeping requirements and reporting of adverse experiences associated with the drug. Drug manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMPs, which impose certain procedural and documentation requirements upon us and our third-party manufacturers. Failure to comply with the statutory and regulatory requirements can subject a manufacturer to possible legal or regulatory action, such as warning letters, suspension of manufacturing, seizure of product, injunctive action or possible civil penalties. We cannot be certain that we or our present or future third-party manufacturers or suppliers will be able to comply with the cGMP regulations and other ongoing FDA regulatory requirements. If our

Table of Contents

present or future third-party manufacturers or suppliers are not able to comply with these requirements, the FDA may halt our clinical trials, require us to recall a drug from distribution, or withdraw approval of the NDA for that drug.

The FDA closely regulates the post-approval marketing and promotion of drugs, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the Internet. A company can make only those claims relating to safety and efficacy that are approved by the FDA. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available drugs for uses that are not described in the drug's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, impose stringent restrictions on manufacturers' communications regarding off-label use.

Competition

The biotechnology and biopharmaceutical industries are rapidly changing and highly competitive. We are seeking to develop and market drug candidates that will compete with other products and therapies that currently exist or are being developed. Other companies are actively seeking to develop products that have disease targets similar to those we are pursuing. We face competition from many different sources, including commercial, pharmaceutical and biotechnology companies, academic institutions, government agencies and private and public research institutions. Many of our competitors have significantly greater financial, manufacturing, marketing and drug development resources than we do. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. Our commercial opportunity will be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer side effects or are less expensive than any products that we may develop. In addition, competitors compete in the areas of recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies and technology licenses.

We believe that it is currently the only company that has an orally available CDK-specific agent in Phase II clinical trials. We believe that several companies are developing drugs targeting cancer that may compete with our candidates. We believe a number of companies, including AstraZeneca, Eisai, Pfizer, Roche, Schering AG, and Sunesis are developing CDK inhibitors in early stage clinical trials in cancer patients. Although Aventis, a predecessor of Sanofi-Aventis, had previously announced that it has ceased Phase II development of alvocidib or flavopiridol, a CDK inhibitor, we believe that the National Cancer Institute's Cancer Therapy Evaluation Program is continuing to enroll patients in a Phase II trial and that Sanofi-Aventis has reinitiated development of alvocidib in Phase III clinical trials in patients with chronic leukemia. Several pharmaceutical and biotechnology companies have nucleoside analogs on the market or in clinical trials for oncology indications, including, Eli Lilly, Genzyme, GlaxoSmithKline and Supergen. A number of companies are pursuing discovery and research activities in each of the other areas that are the subject of our research and drug development programs. We believe that AstraZeneca, Merck, jointly with Vertex, Millennium and Serono have commenced Phase II or Phase I clinical trials of Aurora kinase inhibitors in patients with advanced cancers. Several companies have reported selection of Aurora kinase inhibitor candidates for development and may have started or are expected to start clinical trials within the next twelve months. We believe that Boehringer Ingelheim and Onconova have commenced Phase I or Phase II clinical trials with Plk inhibitor candidates for

oncology indications.

Employees

As of December 31, 2006, we had 58 full-time employees, comprised of 45 employees in research and development and 13 employees in management and finance and administration. From time to time, we also employ independent contractors to support our administrative organizations. We believe we have been successful in attracting skilled and experienced management and scientific personnel. Our employees are not represented by any collective bargaining agreements, and management considers relations with our employees to be good.

Table of Contents

Web Site Access to SEC Filings/Available information

We maintain an Internet website at www.cyclacel.com; however, information found on our website is not incorporated by reference into this report. Through this site, we make available free of charge our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) of the Securities Exchange Act of 1934 as soon as reasonably practicable after we electronically file such material with, or furnish it to, the U.S. Securities and Exchange Commission (SEC). In addition, we publish on our website all reports filed under Section 16(a) of the Exchange Act by our directors, officers and 10% stockholders.

These materials are accessible via the Investor Relations section of our website within the ‘SEC Filings’ link. Some of the information is stored directly on our website, while other information can be accessed by selecting the provided link to the section on the SEC website, which contains filings for our company and its insiders.

Item 1A. Risk Factors

In analyzing our company, you should consider carefully the following risk factors, together with all of the other information included in this annual report on Form 10-K. Factors that could cause or contribute to differences in our actual results include those discussed in the following subsection, as well as those discussed above in ‘Management’s Discussion and Analysis of Financial Condition and Results of Operations’ and elsewhere throughout this annual report on Form 10-K. Each of the following risk factors, either alone or taken together, could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our common stock.

We are at an early stage of development as a company and we do not have, and may never have, any products that generate revenues.

We are at an early stage of development as a company and have a limited operating history on which to evaluate our business and prospects. Since beginning operations in 1997, we have not generated any product revenues. We currently have no products for sale and we cannot guarantee that we will ever have any marketable products. We must demonstrate that our drug candidates satisfy rigorous standards of safety and efficacy for their intended uses before the Food and Drug Administration, or FDA, and other regulatory authorities in the United States, the European Union and elsewhere. Significant additional research, preclinical testing and clinical testing is required before we can file applications with the FDA or other regulatory authorities for premarket approval of our drug candidates. In addition,

to compete effectively, our drugs must be easy to administer, cost-effective and economical to manufacture on a commercial scale. We may not achieve any of these objectives. Seliciclib and sapacitabine, our most advanced drug candidates for the treatment of cancer, are currently our only drug candidates in clinical trials and we cannot be certain that the clinical development of these or any other drug candidates in preclinical testing or clinical development will be successful, that they will receive the regulatory approvals required to commercialize them or that any of our other research and drug discovery programs will yield a drug candidate suitable for investigation through clinical trials. Our commercial revenues, if any, will be derived from sales of drugs that we do not expect to become marketable for several years, if at all.

We have a history of operating losses and we may never become profitable. Our stock is a highly speculative investment.

We have incurred operating losses in each year since beginning operations in 1997 due to costs incurred in connection with our research and development activities and general and administrative costs associated with our operations, and we may never achieve profitability. As of December 31, 2006, our accumulated deficit was $138.3 million. Our net loss from inception through December 31, 2006 was $176.4 million. Our initial drug candidates are in the early stages of clinical testing and we must conduct significant additional clinical trials before we can seek the regulatory approvals necessary to begin commercial sales of our drugs. We expect to incur continued losses for several years, as we continue our research and development of our initial drug candidates, seek regulatory approvals and commercialize

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Table of Contents

any approved drugs. If our initial drug candidates are unsuccessful in clinical trials or we are unable to obtain regulatory approvals, or if our drugs are unsuccessful in the market, we will not be profitable. If we fail to become and remain profitable, or if we are unable to fund our continuing losses, you could lose all or part of your investment.

We will need to raise substantial additional capital to fund our operations and if we fail to obtain additional funding, we may be unable to complete the development and commercialization of our drug candidates or continue our research and development programs.

We have funded all of our operations and capital expenditures with proceeds from the issuance of public equity securities, private placements of our securities, interest on investments, government grants and research and development tax credits. In order to conduct the lengthy and expensive research, preclinical testing and clinical trials necessary to complete the development and marketing of our drug candidates, we will require substantial additional funds. Based on our current operating plans, we expect our existing resources to be sufficient to fund our planned operations for at least the next 12 months. To meet these financing requirements, we may raise funds through public or private equity offerings, debt financings or strategic alliances. Raising additional funds by issuing equity or convertible debt securities will cause our shareholders to experience substantial dilution in their ownership interests and new investors may have rights superior to the rights of our other stockholders. Raising additional funds through debt financing, if available, may involve covenants that restrict our business activities and options. To the extent that we raise additional funds through collaborations and licensing arrangements, we may have to relinquish valuable rights to our drug discovery and other technologies, research programs or drug candidates, or grant licenses on terms that may not be favorable to us. Additional funding may not be available to us on favorable terms, or at all. If we are unable to obtain additional funds, we may be forced to delay or terminate our clinical trials and the development and marketing of our drug candidates.

Clinical trials are expensive, time consuming and subject to delay.

Clinical trials are expensive and complex can take many years and have uncertain outcomes. We estimate that clinical trials of our most advanced drug candidates will continue for several years, but may take significantly longer to complete. The designs used in some of our trials have not been used widely by other pharmaceutical companies. Failure can occur at any stage of the testing and we may experience numerous unforeseen events during, or as a result of, the clinical trial process that could delay or prevent commercialization of our current or future drug candidates, including but not limited to:

- delays in securing clinical investigators or trial sites for our clinical trials;
- delays in obtaining institutional review board, or IRB, and other regulatory approvals to commence a clinical trial;
- slower than anticipated rates of patient recruitment and enrollment, or reaching the targeted number of patients;
- negative or inconclusive results from clinical trials;
- unforeseen safety issues;
- uncertain dosing issues;
- introduction of new therapies or changes in standards of practice or regulatory guidance that render our clinical trial endpoints or the targeting of our proposed indications obsolete;
- inability to monitor patients adequately during or after treatment or problems with investigator or patient compliance with the trial protocols;
- inability to replicate in large controlled studies safety and efficacy data obtained from a limited number of patients in uncontrolled trials; and
- inability or unwillingness of medical investigators to follow our clinical protocols.

If we suffer any significant delays, setbacks or negative results in, or termination of, our clinical trials, we may be unable to continue development of our drug candidates or generate revenue and our development costs could increase significantly.

Table of Contents

Adverse events have been observed in our clinical trials and may force us to stop development of our product candidates or prevent regulatory approval of our product candidates.

Adverse or inconclusive results from our clinical trials may substantially delay, or halt entirely, any further development of our drug candidates. Many companies have failed to demonstrate the safety or effectiveness of drug candidates in later stage clinical trials notwithstanding favorable results in early stage clinical trials. Previously unforeseen and unacceptable side effects could interrupt, delay or halt clinical trials of our drug candidates and could result in the FDA or other regulatory authorities denying approval of our drug candidates. We will need to demonstrate safety and efficacy for specific indications of use, and monitor safety and compliance with clinical trial protocols throughout the development process. To date, long-term safety and efficacy has not been demonstrated in clinical trials for any of our drug candidates. Toxicity and ‘severe adverse effects’ as defined in trial protocols have been noted in preclinical and clinical trials involving certain of our drug candidates. For example, elevations of liver enzymes and decrease in potassium levels have been observed in some patients receiving our lead drug candidate, seliciclib and neutropenia was observed in patients receiving sapacitabine. In addition, we may pursue clinical trials for seliciclib in more than one indication. There is a risk that severe toxicity observed in a trial for one indication

could result in the delay or suspension of all trials involving the same drug candidate. We are currently conducting Phase IIb clinical trials to test the safety and efficacy of seliciclib in the treatment of non small cell lung cancer. Independent investigators are conducting Phase I clinical trials to test the safety of sapacitabine in patients with advanced cancers. If these trials or any future trials are unsuccessful, our business and reputation could be harmed and our share price could be negatively affected.

Even if we believe the data collected from clinical trials of our drug candidates are promising with respect to safety and efficacy, such data may not be deemed sufficient by regulatory authorities to warrant product approval. Clinical data can be interpreted in different ways. Regulatory officials could interpret such data in different ways than we do which could delay, limit or prevent regulatory approval. The FDA, other regulatory authorities or we may suspend or terminate clinical trials at any time. Any failure or significant delay in completing clinical trials for our drug candidates, or in receiving regulatory approval for the commercialization of our drug candidates, may severely harm our business and reputation.

If our understanding of the role played by CDKs or Aurora kinases in regulating the cell cycle is incorrect, this may hinder pursuit of our clinical and regulatory strategy.

We have programs to develop small molecule inhibitors of cyclin dependent kinases (CDK) and Aurora kinases. Our lead drug candidate, seliciclib, is a CDK inhibitor, and CYC116 is an Aurora kinase inhibitor, based on our understanding of CDK and Aurora kinase inhibitors. Although a number of pharmaceutical and biotechnology companies are attempting to develop CDK or Aurora inhibitor drugs for the treatment of cancer, no CDK or Aurora kinase inhibitor has yet reached the market. Our seliciclib program relies on our understanding of the interaction of CDKs with other cellular mechanisms that regulate key stages of cell growth. If our understanding of the role played by CDKs or Aurora kinase inhibitors in regulating the cell cycle is incorrect, our lead drug and CYC116 may fail to produce therapeutically relevant results, hindering our ability to pursue our clinical and regulatory strategy.

If we fail to enter into and maintain successful strategic alliances for our drug candidates, we may have to reduce or delay our drug candidate development or increase our expenditures.

An important element of our strategy for developing, manufacturing and commercializing our drug candidates is entering into strategic alliances with pharmaceutical companies or other industry participants to advance our programs and enable us to maintain our financial and operational capacity.

We face significant competition in seeking appropriate alliances. We may not be able to negotiate alliances on acceptable terms, if at all. In addition, these alliances may be unsuccessful. If we fail to create and maintain suitable alliances, we may have to limit the size or scope of, or delay, one or more of our drug development or research programs. If we elect to fund drug development or research programs on our own, we will have to increase our expenditures and will need to obtain additional funding, which may be unavailable or available only on unfavorable terms.

Table of Contents

We are making extensive use of biomarkers, which are not scientifically validated, and our reliance on biomarker data may thus lead us to direct our resources inefficiently.

We are making extensive use of biomarkers in an effort to facilitate our drug development and to optimize our clinical trials. Biomarkers are proteins or other substances whose presence in the blood can serve as an indicator of specific cell processes. We believe that these biological markers serve a useful purpose in helping us to evaluate whether our drug candidates are having their intended effects through their assumed mechanisms, and thus enable us to identify more promising drug candidates at an early stage and to direct our resources efficiently. We also believe that biomarkers may eventually allow us to improve patient selection in connection with clinical trials and monitor patient compliance with trial protocols.

For most purposes, however, biomarkers have not been scientifically validated. If our understanding and use of biomarkers is inaccurate or flawed, or if our reliance on them is otherwise misplaced, then we will not only fail to realize any benefits from using biomarkers, but may also be led to invest time and financial resources inefficiently in attempting to develop inappropriate drug candidates. Moreover, although the FDA has issued for comment a draft guidance document on the potential use of biomarker data in clinical development, such data are not currently accepted by the FDA or other regulatory agencies in the United States, the European Union or elsewhere in applications for regulatory approval of drug candidates and there is no guarantee that such data will ever be accepted by the relevant authorities in this connection. Our biomarker data should not be interpreted as evidence of efficacy.

To the extent we elect to fund the development of a drug candidate or the commercialization of a drug at our expense, we will need substantial additional funding.

We plan to market drugs on our own, with or without a partner, that can be effectively commercialized and sold in concentrated markets that do not require a large sales force to be competitive. To achieve this goal, we will need to establish our own specialized sales force, marketing organization and supporting distribution capabilities. The development and commercialization of our drug candidates is very expensive. To the extent we elect to fund the full development of a drug candidate or the commercialization of a drug at our expense, we will need to raise substantial additional funding to:

- fund research and development and clinical trials connected with our research;
- fund clinical trials and seek regulatory approvals;
- build or access manufacturing and commercialization capabilities;
- implement additional internal control systems and infrastructure;
- commercialize and secure coverage, payment and reimbursement of our drug candidates, if any such candidates receive regulatory approval;
- maintain, defend and expand the scope of our intellectual property; and
- hire additional management and scientific personnel.

Our future funding requirements will depend on many factors, including:

- the scope, rate of progress and cost of our clinical trials and other research and development activities;
- the costs and timing of seeking and obtaining regulatory approvals;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;
- the costs associated with establishing sales and marketing capabilities;
- the costs of acquiring or investing in businesses, products and technologies;
- the effect of competing technological and market developments; and
- the payment, other terms and timing of any strategic alliance, licensing or other arrangements that we may establish.

Table of Contents

If we are not able to secure additional funding when needed, we may have to delay, reduce the scope of or eliminate one or more of our clinical trials or research and development programs or future commercialization efforts.

Due to our reliance on contract research organizations or other third parties to conduct clinical trials, we are unable to directly control the timing, conduct and expense of our clinical trials.

We do not have the ability to independently conduct clinical trials required to obtain regulatory approvals for our drug candidates. We must rely on third parties, such as contract research organizations, medical institutions, clinical investigators and contract laboratories to conduct our clinical trials. In addition, we rely on third parties to assist with our preclinical development of drug candidates. 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 our drug candidates.

To the extent we are able to enter into collaborative arrangements or strategic alliances, we will be exposed to risks related to those collaborations and alliances.

Although we are not currently party to any collaboration arrangement or strategic alliance that is material to our business, in the future we expect to be dependent upon collaborative arrangements or strategic alliances to complete the development and commercialization of some of our drug candidates particularly after the Phase II stage of clinical testing. These arrangements may place the development of our drug candidates outside our control, may require us to relinquish important rights or may otherwise be on terms unfavorable to us.

We may be unable to locate and enter into favorable agreements with third parties, which could delay or impair our ability to develop and commercialize our drug candidates and could increase our costs of development and commercialization. Dependence on collaborative arrangements or strategic alliances will subject us to a number of risks, including the risk that:

- we may not be able to control the amount and timing of resources that our collaborators may devote to the drug candidates;
- our collaborators may experience financial difficulties;
- we may be required to relinquish important rights such as marketing and distribution rights;
- business combinations or significant changes in a collaborator’s business strategy may also adversely affect a collaborator’s willingness or ability to complete our 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; and
- collaborative arrangements are often terminated or allowed to expire, which would delay the development and may increase the cost of developing our drug candidates.

We have no manufacturing capacity and will rely on third party manufacturers for the late stage development and commercialization of any drugs we may develop.

We do not currently operate manufacturing facilities for clinical or commercial production of our drug candidates under development. We currently lack the resources or the capacity to manufacture any of our products on a clinical or

commercial scale. We anticipate future reliance on a limited number of third party manufacturers until we are able to expand our operations to include manufacturing capacities. Any performance failure on the part of future manufacturers could delay late stage clinical development or regulatory approval of our drug candidates or commercialization of our drugs, producing additional losses and depriving us of potential product revenues.

Table of Contents

If the FDA or other regulatory agencies approve any of our drug candidates for commercial sale, or if we significantly expand our clinical trials, we will need to manufacture them in larger quantities. To date, our drug candidates have been manufactured in small quantities for preclinical testing and clinical trials and we may not be able to successfully increase the manufacturing capacity, whether in collaboration with third party manufacturers or on our own, for any of our drug candidates in a timely or economic manner, or at all. For example, the manufacture of our drug candidate sapacitabine and CYC116 require several steps and it is not known if scale up to commercial production is feasible. Significant scale-up of manufacturing may require additional validation studies, which the FDA and other regulatory bodies must review and approve. If we are unable to successfully increase the manufacturing capacity for a drug candidate whether for late stage clinical trials or for commercial sale, the drug development, regulatory approval or commercial launch of any related drugs may be delayed or there may be a shortage in supply. Even if any third party manufacturer makes improvements in the manufacturing process for our drug candidates, we may not own, or may have to share, the intellectual property rights to such innovation.

We currently have no marketing or sales staff. If we are unable to conclude strategic alliances with marketing partners or if we are unable to develop our own sales and marketing capabilities, we may not be successful in commercializing any drugs we may develop.

Our strategy is to develop compounds through the Phase II stage of clinical testing and market or co-promote certain of our drugs on our own. We have no sales, marketing or distribution capabilities. We will depend primarily on strategic alliances with third parties, which have established distribution systems and sales forces, to commercialize our drugs. To the extent that we are unsuccessful in commercializing any drugs ourselves or through a strategic alliance, product revenues will suffer, we will incur significant additional losses and our share price will be negatively affected.

If we evolve from a company primarily involved in discovery and development to one also involved in the commercialization of drugs, we may encounter difficulties in managing our growth and expanding our operations successfully.

If we advance our drug candidates through clinical trials, we will need to expand our development and regulatory capabilities and develop manufacturing, marketing and sales capabilities or contract with third parties to provide these capabilities for us. If our operations expand, we expect that we will need to manage additional relationships with various collaborative partners, suppliers and other third parties. Our ability to manage our operations and any growth will require us to make appropriate changes and upgrades (as necessary) to our operational, financial and management controls, reporting systems and procedures where we may operate. Any inability to manage growth could delay the execution of our business plan or disrupt our operations.

The failure to attract and retain skilled personnel could impair our drug development and commercialization efforts.

We are highly dependent on our senior management and key scientific and technical personnel. The loss of the services of any member of our senior management, scientific or technical staff may significantly delay or prevent the achievement of drug development and other business objectives and could have a material adverse effect on our business, operating results and financial condition. We also rely on consultants and advisors to assist us in formulating our research and development strategy. All of our consultants and advisors are either self-employed or employed by other organizations, and they may have conflicts of interest or other commitments, such as consulting or advisory contracts with other organizations, that may affect their ability to contribute to us.

We intend to expand and develop new drug candidates. We will need to hire additional employees in order to continue our clinical trials and market our drug candidates. This strategy will require us to recruit additional executive management and scientific and technical personnel. There is currently intense competition for skilled executives and employees with relevant scientific and technical expertise, and this competition is likely to continue. The inability to attract and retain sufficient scientific, technical and managerial personnel could limit or delay our product development efforts, which would adversely affect the development of our drug candidates and commercialization of our potential drugs and growth of our business.

Table of Contents

Our drug candidates are subject to extensive regulation, which can be costly and time-consuming, and we may not obtain approvals for the commercialization of any of our drug candidates.

The clinical development, manufacturing, selling and marketing of our drug candidates are subject to extensive regulation by the FDA and other regulatory authorities in the United States, the European Union and elsewhere. These regulations also vary in important, meaningful ways from country to country. We are not permitted to market a potential drug in the United States until we receive approval of a New Drug Application, or NDA, from the FDA. We have not received an NDA approval from the FDA for any of our drug candidates.

Obtaining an NDA approval is expensive and is a complex, lengthy and uncertain process. The FDA approval process for a new drug involves completion of preclinical studies and the submission of the results of these studies to the FDA, together with proposed clinical protocols, manufacturing information, analytical data and other information in an Investigational New Drug application, or IND, which must become effective before human clinical trials may begin. Clinical development typically involves three phases of study: Phase I, II and III. The most significant costs associated with clinical development are the Phase III clinical trials as they tend to be the longest and largest studies conducted during the drug development process. After completion of clinical trials, an NDA may be submitted to the FDA. In responding to an NDA, the FDA may refuse to file the application, or if accepted for filing, the FDA may grant marketing approval, request additional information or deny the application if it determines that the application does not provide an adequate basis for approval. In addition, failure to comply with FDA and other applicable foreign and U.S. regulatory requirements may subject it to administrative or judicially imposed sanctions. These include warning letters, civil and criminal penalties, injunctions, product seizure or detention, product recalls, total or partial suspension of production and refusal to approve either pending NDAs, or supplements to approved NDAs.

Despite the substantial time and expense invested in preparation and submission of an NDA or equivalents in other jurisdictions, regulatory approval is never guaranteed. The FDA and other regulatory authorities in the United States, the European Union and elsewhere exercise substantial discretion in the drug approval process. The number, size and design of preclinical studies and clinical trials that will be required for FDA or other regulatory approval will vary depending on the drug candidate, the disease or condition for which the drug candidate is intended to be used and the

regulations and guidance documents applicable to any particular drug candidate. The FDA or other regulators can delay, limit or deny approval of a drug candidate for many reasons, including, but not limited to:

- those discussed in the risk factor which immediately follows;
- the fact that FDA or other regulatory officials may not approve our or our third party manufacturer's processes or facilities; or
- the fact that new regulations may be enacted by the FDA or other regulators may change their approval policies or adopt new regulations requiring new or different evidence of safety and efficacy for the intended use of a drug candidate.

Following regulatory approval of any drug candidate, we would be subject to ongoing regulatory obligations and restrictions, which may result in significant expense and limit our ability to commercialize our potential drugs.

If one of our drug candidates is approved by the FDA or by another regulatory authority, we would be held to extensive regulatory requirements over product manufacturing, labeling, packaging, adverse event reporting, storage, advertising, promotion and record keeping. Regulatory approvals may also be subject to significant limitations on the indicated uses or marketing of the drug candidates. Potentially costly follow-up or post-marketing clinical studies may be required as a condition of approval to further substantiate safety or efficacy, or to investigate specific issues of interest to the regulatory authority. Previously unknown problems with the drug candidate, including adverse events of unanticipated severity or frequency, may result in restrictions on the marketing of the drug, and could include withdrawal of the drug from the market.

In addition, the law or regulatory policies governing pharmaceuticals may change. New statutory requirements may be enacted or additional regulations may be enacted that could prevent or delay

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Table of Contents

regulatory approval of our drug candidates. We cannot predict the likelihood, nature or extent of adverse government regulation that may arise from future legislation or administrative action, either in the United States or elsewhere. If we are not able to maintain regulatory compliance, it might not be permitted to market our drugs and our business could suffer.

Our applications for regulatory approval could be delayed or denied due to problems with studies conducted before we in-licensed some of our product candidates.

We currently license some of the compounds and drug candidates used in our research programs from third parties. These include sapacitabine, licensed from Sankyo Co., Ltd and CYC381 and related intellectual property, licensed from Lorus Therapeutics, Inc. Our present research involving these compounds relies upon previous research conducted by third parties over whom we had no control and before we in-licensed the drug candidates. In order to receive regulatory approval of a drug candidate, we must present all relevant data and information obtained during our research and development, including research conducted prior to our licensure of the drug candidate. Although we are not currently aware of any such problems, any problems that emerge with preclinical research and testing conducted prior to our in-licensing may affect future results or our ability to document prior research and to conduct clinical trials, which could delay, limit or prevent regulatory approval for our drug candidates.

We face intense competition and our competitors may develop drugs that are less expensive, safer, or more effective

than our drug candidates.

We are engaged in a rapidly changing and highly competitive field. We are seeking to develop and market products that will compete with other products and drugs that currently exist or are being developed. We compete with companies that are developing small molecule drugs, as well as companies that have developed drugs or are developing alternative drug candidates for cancer or other serious disorders where there is abnormal cell proliferation. We believe that other companies are currently developing drugs targeting cancer that may compete with our drug candidates, including AstraZeneca, Eisai, Pfizer, Roche, Schering AG, and Sunesis. Although Aventis, a predecessor of Sanofi-Aventis, had previously announced that it has ceased Phase II development of alvocidib or flavopiridol, a CDK inhibitor, we believe that the National Cancer Institute's Cancer Therapy Evaluation Program is continuing to enroll patients in a Phase II trial and that Sanofi-Aventis has reinitiated development of alvocidib in Phase III clinical trials in patients with chronic leukemia. Several pharmaceutical and biotechnology companies have nucleoside analogs on the market or in clinical trials for oncology indications, including Eli Lilly, Genzyme, GlaxoSmithKline and Supergen. A number of companies are pursuing discovery and research activities in each of the other areas that are the subject of our research and drug development programs. We believe that AstraZeneca, Merck, jointly with Vertex, Millennium and Serono have commenced Phase II or Phase I clinical trials of Aurora kinase inhibitors in patients with advanced cancers. Several companies have reported selection of Aurora kinase inhibitor candidates for development and may have started or are expected to start clinical trials within the next twelve months. We believe that Boehringer Ingelheim and Onconova have commenced Phase I or Phase II clinical trials with Plk inhibitor candidates for oncology indications.

Our competitors, either alone or together with collaborators, may have substantially greater financial resources and research and development staff. Our competitors may also have more experience:

- developing drug candidates;
- conducting preclinical and clinical trials;
- obtaining regulatory approvals; and
- commercializing drug candidates.

Our competitors may succeed in obtaining patent protection and regulatory approval and may market drugs before we do. If our competitors market drugs that are less expensive, safer, more effective or more convenient to administer than our potential drugs, or that reach the market sooner than our potential drugs, we may not achieve commercial success. Scientific, clinical or technical developments by

Table of Contents

our competitors may render our drug candidates obsolete or noncompetitive. We anticipate that we will face increased competition in the future as new companies enter the markets and as scientific developments progress. If our drug candidates obtain regulatory approvals, but do not compete effectively in the marketplace, our business will suffer.

The commercial success of our drug candidates depends upon their market acceptance among physicians, patients, healthcare providers and payors and the medical community.

If our drug candidates are approved by the FDA or by another regulatory authority, the resulting drugs, if any, may not gain market acceptance among physicians, healthcare providers and payors, patients and the medical community. The degree of market acceptance of any of our approved drugs will depend on a variety of factors, including:

- timing of market introduction, number and clinical profile of competitive drugs;
- our ability to provide acceptable evidence of safety and efficacy;
- relative convenience and ease of administration;
- cost-effectiveness;
- availability of coverage, reimbursement and adequate payment from health maintenance organizations and other third party payors;
- prevalence and severity of adverse side effects; and
- other potential advantages over alternative treatment methods.

If our drugs fail to achieve market acceptance, we may not be able to generate significant revenue and our business would suffer.

There is uncertainty related to coverage, reimbursement and payment by healthcare providers and payors for newly approved drugs. The inability or failure to obtain coverage could affect our ability to market our future drugs and decrease our ability to generate revenue.

The availability and levels of coverage and reimbursement of newly approved drugs by healthcare providers and payors is subject to significant uncertainty. The commercial success of our drug candidates in both the U.S. and international markets is substantially dependent on whether third party coverage and reimbursement is available. The U.S. Centers for Medicare and Medicaid Services, health maintenance organizations and other third party payors in the United States, the European Union and other jurisdictions are increasingly attempting to contain healthcare costs by limiting both coverage and the level of reimbursement of new drugs and, as a result, they may not cover or provide adequate payment for our potential drugs. Our drug candidates may not be considered cost-effective and reimbursement may not be available to consumers or may not be sufficient to allow our drug candidates to be marketed on a competitive basis.

In some countries, pricing of prescription drugs is subject to government control. In such countries, pricing negotiations with governmental authorities can take three to 12 months or longer following application to the competent authorities. To obtain reimbursement or pricing approval in such countries may require conducting an additional clinical trial comparing the cost-effectiveness of the drug to other alternatives. In the United States, the Medicare Part D drug benefit to be implemented in 2006 will limit drug coverage through formularies and other cost and utilization management programs, while Medicare Part B limits drug payments to a certain percentage of average price or through restrictive payment policies of ‘least costly alternatives’ and ‘inherent reasonableness.’ Our business could be materially harmed if coverage, reimbursement or pricing is unavailable or set at unsatisfactory levels.

We may be exposed to product liability claims that may damage our reputation and may not be able to obtain adequate insurance.

Because we conduct clinical trials in humans, we face the risk that the use of our drug candidates will result in adverse effects. We believe that we have obtained reasonably adequate product liability

Table of Contents

insurance coverage for our trials. We cannot predict, however, the possible harm or side effects that may result from our clinical trials. Such claims may damage our reputation and we may not have sufficient resources to pay for any liabilities resulting from a claim excluded from, or beyond the limit of, our insurance coverage.

Once we have commercially available drugs based on our drug candidates, we will be exposed to the risk of product liability claims. This risk exists even with respect to those drugs that are approved for commercial sale by the FDA or other regulatory authorities in the United States, the European Union or elsewhere and manufactured in facilities licensed and regulated by the FDA or other such regulatory authorities. We intend to secure limited product liability insurance coverage, but may not be able to obtain such insurance on acceptable terms with adequate coverage, or at reasonable cost. There is also a risk that third parties that we have agreed to indemnify could incur liability. Even if we were ultimately successful in product liability litigation, the litigation would consume substantial amounts of our financial and managerial resources and may create adverse publicity, all of which would impair our ability to generate sales of the litigated product as well as our other potential drugs.

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

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject to claims that these employees 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. If we fail in defending such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. A loss of key research personnel or their work product could hamper or prevent our ability to commercialize certain potential drugs, which could severely harm our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

Defending against claims relating to improper handling, storage or disposal of hazardous chemical, radioactive or biological materials could be time consuming and expensive.

Our research and development involves the controlled use of hazardous materials, including chemicals, radioactive and biological materials such as chemical solvents, phosphorus and bacteria. Our operations produce hazardous waste products. We cannot eliminate the risk of accidental contamination or discharge and any resultant injury from those materials. Various laws and regulations govern the use, manufacture, storage, handling and disposal of hazardous materials. We may be sued for any injury or contamination that results from our use or the use by third parties of these materials. Compliance with environmental laws and regulations may be expensive, and current or future environmental regulations may impair our research, development and production efforts.

If we fail to enforce adequately or defend our intellectual property rights our business may be harmed.

Our commercial success depends in large part on obtaining and maintaining patent and trade secret protection for our drug candidates, the methods used to manufacture those drug candidates and the methods for treating patients using those drug candidates. Specifically our two lead drug candidates have composition of matter patents that expire at the earliest case in 2016 and 2014. Failure to obtain, maintain or extend the patents could adversely affect our business. We will only be able to protect our drug candidates and our technologies from unauthorized use by third parties to the extent that valid and enforceable patents or trade secrets cover them.

Our ability to obtain patents is uncertain because legal means afford only limited protections and may not adequately protect our rights or permit it to gain or keep any competitive advantage. Some legal principles remain unresolved and the breadth or interpretation of claims allowed in patents in the United States, the European Union or elsewhere can still be difficult to ascertain or predict. In addition, the specific content of patents and patent applications that are necessary to support and interpret patent

Table of Contents

claims is highly uncertain due to the complex nature of the relevant legal, scientific and factual issues. Changes in either patent laws or in interpretations of patent laws in the United States, the European Union or elsewhere may diminish the value of our intellectual property or narrow the scope of our patent protection. 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 and technologies. In addition, we generally do not control the patent prosecution of subject matter that we license from others and have not controlled the earlier stages of the patent prosecution. Accordingly, we are unable to exercise the same degree of control over this intellectual property as we would over our own.

Even if patents are issued regarding our drug candidates or methods of using them, those patents can be challenged by our competitors who may argue such patents are invalid and/or unenforceable. Patents also will not protect our drug candidates if competitors devise ways of making or using these product candidates without legally infringing our patents. The U.S. Federal Food, Drug and Cosmetic, or FD&C, Act and FDA regulations and policies and equivalents in other jurisdictions provide incentives to manufacturers to challenge patent validity or create modified, noninfringing versions of a drug in order to facilitate the approval of abbreviated new drug applications for generic substitutes. These same types of incentives encourage manufacturers to submit new drug applications that rely on literature and clinical data not prepared for or by the drug sponsor.

Proprietary trade secrets and unpatented know-how are also very important to our business. We rely on trade secrets to protect our technology, especially where we do not believe that patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. Our employees, consultants, contractors, outside scientific collaborators and other advisors may unintentionally or willfully disclose our confidential information to competitors, and confidentiality agreements may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. Enforcing a claim that a third party obtained illegally and is using trade secrets is expensive and time consuming, and the outcome is unpredictable. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how. Failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

If we infringe intellectual property rights of third parties, we may increase our costs or be prevented from being able to commercialize our drug candidates.

There is a risk that we may have infringed, are infringing or will infringe the proprietary rights of third parties because patents and pending applications belonging to third parties exist in the United States, the European Union and elsewhere in the world in the areas our research explores. Others might have been the first to make the inventions covered by each of our or our licensors' pending patent applications and issued patents and might have been the first to file patent applications for these inventions. In addition, because the patent application process can take several years to complete, there may be currently pending applications, unknown to us, which may later result in issued patents that cover the production, manufacture, commercialization or use of our drug candidates. In addition, the production, manufacture, commercialization or use of our product candidates may infringe existing patents of which we are not aware. Numerous third-party United States and foreign issued patents and pending applications exist in the area of kinases, including CDK, Aurora and Plk for which we have research programs. Because patent applications can take several years to issue, there may be pending applications that may result in issued patents that cover our technologies or product candidates. For example, some pending patent applications contain broad claims that could represent freedom to operate limitations for some of our kinase programs should they be issued unchanged. If we wish to use the technology or compound claimed in issued and unexpired patents owned by others, we will need to obtain a license from the owner, enter into litigation and/or challenge the validity of the patents or incur the risk of litigation in the event that the owner asserts that we infringe its patents. In one case we have opposed a European patent relating to

human aurora kinase. We are also aware of a corresponding U.S. patent containing method of treatment claims for specific cancers using aurora kinase modulators which, if held valid, could potentially restrict the use of certain of our aurora kinase inhibitors once clinical trials are completed.

Table of Contents

There has been substantial litigation and other proceedings regarding patent and other intellectual property rights in the pharmaceutical and biotechnology industries. Defending against third party claims, including litigation in particular, would be costly and time consuming and would divert management's attention from our business, which could lead to delays in our development or commercialization efforts. If third parties are successful in their claims, we might have to pay substantial damages or take other actions that are adverse to our business. As a result of intellectual property infringement claims, or to avoid potential claims, we might:

- be prohibited from selling or licensing any product that we may develop unless the patent holder licenses the patent to us, which it is not required to do;
- be required to pay substantial royalties or grant a cross license to our patents to another patent holder;
- decide to move some of our screening work outside Europe;
- be required to pay substantial damages for past infringement, which we may have to pay if a court determines that our product candidates or technologies infringe a competitor's patent or other proprietary rights; or
- be required to redesign the formulation of a drug candidate so it does not infringe, which may not be possible or could require substantial funds and time.

The development programs for our two lead drug candidates are based in part on intellectual property rights we license from others, and any termination of those licenses could seriously harm our business.

We have in-licensed certain patent rights in connection with the development programs for each of our two lead drug candidates. With respect to seliciclib, we hold a license from Centre National de Recherche Scientifique, or CNRS, and Institut Curie. With respect to sapacitabine, we hold a license from Sankyo Co., Ltd. of Japan. Both of these license agreements impose payment and other material obligations on us. Under the CNRS/Institut Curie license, we are obligated to pay license fees, milestone payments and royalties. We are also obligated to use reasonable efforts to develop and commercialize products based on the licensed patents. Under the Sankyo license, we are obligated to pay license fees, milestone payments and royalties. We are also obligated to use commercially reasonable efforts to commercialize products based on the licensed rights and to use reasonable efforts to obtain regulatory approval to sell the products in at least one country by September 2011. Although we are currently in compliance with all of our material obligations under these licenses, if we were to breach any such obligations our counterparties would be permitted to terminate the licenses. This would restrict or delay or eliminate our ability to develop and commercialize these drug candidates, which could seriously harm our business.

Intellectual property rights of third parties could adversely affect our ability to commercialize our drug candidates.

If patents issued to third parties contain valid claims that cover our compounds or their manufacture or uses relevant to our development plans, we may be required to obtain licenses to these patents or to develop or obtain alternative technology. We are aware of several published patent applications, and understand that others may exist, that could support claims that, if granted, could cover various aspects of our developmental programs, including in some cases

particular uses of our lead drug candidate, seliciclib, sapacitabine or other therapeutic candidates, or gene sequences and techniques that we use in the course of our research and development. In addition, we understand that other applications exist relating to potential uses of seliciclib and sapacitabine that are not part of our current clinical programs for these compounds. Although we intend to continue to monitor these applications, we cannot predict what claims will ultimately be allowed and if allowed what their scope would be. If a patent is issued that covers our compounds or their manufacture or uses or screening assays related to our development plans then we may not be in a position to commercialize the related drug candidate unless we successfully pursue litigation to have that patent invalidated or enter into a licensing arrangement with the patent holder. Any such litigation would be time consuming and costly, and our outcome would not be

Table of Contents

guaranteed, and we cannot be certain that we would be able to enter into a licensing arrangement with the patent holder on commercially reasonable terms. In either case, our business prospects could be materially adversely affected. In one case we have opposed a granted European patent relatetd to human aurora kinase. We are also aware of a corresponding US patent containing method of treatment claims for specific cancers using aurora kinase modulators, which if held valid, could potentially restrict the use of certain of our aurora kinase inhibitors.

We have limited experience attempting to comply with public company obligations. Attempting to comply with these requirements will increase our costs and require additional management resources, and we still may fail to comply.

As a newly public company, we face and will continue to face increased legal, accounting, administrative and other costs and expenses as a public company that we did not incur as a private company. Compliance with the Sarbanes Oxley Act of 2002, as well as other rules of the SEC, the Public Company Accounting Oversight Board and The Nasdaq Global Market has resulted in a significant initial cost to us as well as an ongoing increase in our legal, audit and financial compliance costs. As a public company, we are subject to Section 404 of the Sarbanes Oxley Act relating to internal control over financial reporting. We have completed a formal process to evaluate our internal controls for purposes of Section 404, and we can conclude that our internal control over financial reporting is effective.

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. If we cannot provide reliable financial reports or prevent fraud, our operating results could be harmed. We have completed a formal process to evaluate our internal control over financial reporting. However, guidance from regulatory authorities in the area of internal controls continues to evolve and substantial uncertainty exists regarding our on-going ability to comply by applicable deadlines. Any failure to implement required new or improved controls, or difficulties encountered in their implementation, could harm our operating results or cause us to fail to meet our reporting obligations. Ineffective internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our common stock.

Our common stock may have a volatile public trading price.

An active public market for our common stock has not developed. Our stock can trade in small volumes which may make the price of our stock highly volatile. The last reported price of our stock may not represent the price at which you would be able to buy or sell the stock. The market prices for securities of companies comparable to us have been highly volatile. Often, these stocks have experienced significant price and volume fluctuations for reasons unrelated to

the operating performance of the individual companies. Factors giving rise to this volatility may include:

- disclosure of actual or potential clinical results with respect to product candidates we are developing;
- regulatory developments in both the United States and abroad;
- developments concerning proprietary rights, including patents and litigation matters;
- public concern about the safety or efficacy of our product candidates or technology, or related technology, or new technologies generally;
- concern about the safety or efficacy of our product candidates or technology, or related technology, or new technologies generally;
- public announcements by our competitors or others; and
- general market conditions and comments by securities analysts and investors.

Fluctuations in our operating losses could adversely affect the price of our common stock.

Our operating losses may fluctuate significantly on a quarterly basis. Some of the factors that may cause our operating losses to fluctuate on a period-to-period basis include the status of our preclinical and

Table of Contents

clinical development programs, level of expenses incurred in connection with our preclinical and clinical development programs, implementation or termination of collaboration, licensing, manufacturing or other material agreements with third parties, non-recurring revenue or expenses under any such agreement, and compliance with regulatory requirements. Period-to-period comparisons of our historical and future financial results may not be meaningful, and investors should not rely on them as an indication of future performance. Our fluctuating losses may fail to meet the expectations of securities analysts or investors. Our failure to meet these expectations may cause the price of our common stock to decline.

Anti-takeover provisions in our charter documents and provisions of Delaware law may make an acquisition more difficult and could result in the entrenchment of management.

We are incorporated in Delaware. Anti-takeover provisions of Delaware law and our amended and restated certificate of incorporation and amended and restated bylaws may make a change in control or efforts to remove management more difficult. Also, under Delaware law, our board of directors may adopt additional anti-takeover measures.

We have the authority to issue up to 5,000,000 shares of preferred stock and to determine the terms of those shares of stock without any further action by our stockholders. If the board of directors exercises this power to issue preferred stock, it could be more difficult for a third party to acquire a majority of our outstanding voting stock and vote the stock they acquire to remove management or directors.

Our amended and restated certificate of incorporation and amended and restated bylaws also provides staggered terms for the members of our board of directors. Under Section 141 of the Delaware General Corporation Law, our directors may be removed by stockholders only for cause and only by vote of the holders of a majority of voting shares then outstanding. These provisions may prevent stockholders from replacing the entire board in a single proxy contest, making it more difficult for a third party to acquire control of us without the consent of our board of directors. These provisions could also delay the removal of management by the board of directors with or without cause. In addition,

our directors may only be removed for cause and amended and restated bylaws limit the ability our stockholders to call special meetings of stockholders.

Under Section 203 of the Delaware General Corporation Law, a corporation may not engage in a business combination with any holder of 15% or more of its capital stock until the holder has held the stock for three years unless, among other possibilities, the board of directors approves the transaction. Our board of directors could use this provision to prevent changes in management. The existence of the foregoing provisions could limit the price that investors might be willing to pay in the future for shares of our common stock

Our certificate of incorporation and bylaws and certain provisions of Delaware law may delay or prevent a change in our management and make it more difficult for a third party to acquire us.

Our certificate of incorporation and bylaws contain provisions that could delay or prevent a change in our board of directors and management teams. Some of these provisions:

- authorize the issuance of preferred stock that can be created and issued by the board of directors without prior stockholder approval, commonly referred to as ‘blank check’ preferred stock, with rights senior to those of our common stock;
- provide for the board of directors to be divided into three classes; and
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit stockholder action by written consent.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of large stockholders to complete a business combination with, or acquisition of, us. These provisions may prevent a business combination or acquisition that would be attractive to stockholders and could limit the price that investors would be willing to pay in the future for our stock.

These provisions also make it more difficult for our stockholders to replace members of our board of directors. Because our board of directors is responsible for appointing the members of our management

Table of Contents

team, these provisions could in turn affect any attempt to replace our current management team. Additionally, these provisions may prevent an acquisition that would be attractive to stockholders and could limit the price that investors would be willing to pay in the future for our common stock.

We may have limited ability to pay cash dividends on the convertible preferred stock.

Delaware law may limit our ability to pay cash dividends on the convertible preferred stock. Under Delaware law, cash dividends on our capital stock may only be paid from ‘surplus’ or, if there is no ‘surplus,’ from the corporation’s net profits for the current or preceding fiscal year. Delaware law defines ‘surplus’ as the amount by which the total assets of a corporation, after subtracting its total liabilities, exceed the corporation’s capital, as determined by its board of directors. Since we are not profitable, our ability to pay cash dividends will require the availability of adequate surplus. Even if adequate surplus is available to pay cash dividends on the convertible preferred stock, we may not have sufficient cash to pay dividends on the convertible preferred stock. If that was to happen, holders of preferred stock would be granted certain additional rights until such dividends were repaid.

Our common and convertible preferred stock may experience extreme price and volume fluctuations, which could lead to costly litigation for the Company and make an investment in the Company less appealing.

The market price of our common and convertible preferred stock may fluctuate substantially due to a variety of factors, including:

- additions to or departures of our key personnel;
- announcements of technological innovations or new products or services by us or our competitors;
- announcements concerning our competitors or the biotechnology industry in general;
- new regulatory pronouncements and changes in regulatory guidelines;
- general and industry-specific economic conditions;
- changes in financial estimates or recommendations by securities analysts;
- variations in our quarterly results;
- announcements about our collaborators or licensors; and
- changes in accounting principles.

The market prices of the securities of biotechnology companies, particularly companies like us without product revenues and earnings, have been highly volatile and are likely to remain highly volatile in the future. This volatility has often been unrelated to the performance of particular companies. In the past, companies that experience volatility in the market price of their securities have often faced securities class action litigation. Moreover, market prices for stocks of biotechnology-related and technology companies frequently reach levels that bear no relationship to the performance of these companies. These market prices generally are not sustainable and are highly volatile. Whether or not meritorious, litigation brought against us could result in substantial costs, divert our management's attention and resources and harm our financial condition and results of operations.

The future sale of our common and convertible preferred stock, and future issuances of our common stock upon conversion of our convertible preferred stock and upon the payment of make-whole dividends, if any, could negatively affect our stock price.

If our common or convertible preferred stockholders sell substantial amounts of its stock in the public market, or the market perceives that such sales may occur, the market price of our common and convertible preferred stock could fall.

In addition, if we exercise our rights to pay make-whole dividends in common stock rather than in cash upon conversion of our convertible preferred stock to common stock, then the sale of such shares of

Table of Contents

common stock or the perception that such sales may occur could cause the market price of our stock to fall. Additionally, after our convertible preferred stock offering, the holders of our convertible preferred stock had the right to convert each share of convertible preferred stock into approximately 0.42553 shares of our common stock. Such conversion rate is subject to certain antidilution adjustments that, upon the occurrence of certain events, will increase the number of shares of common stock that each holder of convertible preferred stock will receive upon conversion into common stock. Such antidilution price adjustments may apply in the case of any strategic alternative that we pursue which may result in further dilution to the holders of outstanding common stock. The conversion of our

convertible preferred stock into common stock and the payment of any make-whole dividends in shares of common stock in lieu of cash, may result in substantial dilution to the interests of our holders of common stock.

If we exchange the convertible preferred stock for debentures, the exchange will be taxable but we will not provide any cash to pay any tax liability that any convertible preferred stockholder may incur.

An exchange of convertible preferred stock for debentures, as well as any dividend make-whole or interest make-whole payments paid in our common stock, will be taxable events for U.S. federal income tax purposes, which may result in tax liability for the holder of convertible preferred stock without any corresponding receipt of cash by the holder. In addition, the debentures may be treated as having original issue discount, a portion of which would generally be required to be included in the holder's gross income even though the cash to which such income is attributable would not be received until maturity or redemption of the debenture. We will not distribute any cash to you to pay these potential tax liabilities.

If we automatically convert the convertible preferred stock, there is a substantial risk of fluctuation in the price of our common stock from the date we elect to automatically convert to the conversion date.

We may elect to automatically convert the convertible preferred stock on or prior to maturity if our common stock price has exceeded 150% of the conversion price for at least 20 trading days during a 30-day trading period ending within five trading days prior to the notice of automatic conversion. You should be aware that there is a risk of fluctuation in the price of our common stock between the time when we may first elect to automatically convert the preferred and the automatic conversion date.

We do not intend to pay cash dividends on our common stock in the foreseeable future.

We do not anticipate paying cash dividends on our common stock in the foreseeable future. Any payment of cash dividends will depend on our financial condition, results of operations, capital requirements, the outcome of the review of our strategic alternatives and other factors and will be at the discretion of our board of directors. Accordingly, investors will have to rely on capital appreciation, if any, to earn a return on their investment in our common stock. Furthermore, we may in the future become subject to contractual restrictions on, or prohibitions against, the payment of dividends.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

In October 2006, we entered into a five-year lease for office space of approximately 6,500 square feet in Berkeley Heights, New Jersey which is the location of our corporate headquarters.

In October 2000, we entered into a 25-year lease for our research and development facility in Dundee, Scotland. We also leased a second research facility at the Babraham Research Campus, Cambridge, England. We entered into this five-year lease in August 2005. There is an option to terminate the lease on July 31, 2007 at a cost to the Company of $104,000.

Additionally, we leased a total of approximately 52,100 square feet of space at two former Xcyte facilities. The Company leased approximately 11,600 square feet of office space in Seattle, Washington, with monthly payments of approximately $19,000. The lease on this space expired in September 2006, and

Table of Contents

we have not renewed the lease. We also lease approximately 40,500 square feet of space in Bothell, Washington, with monthly payments of approximately $80,000. The lease term on this space expires December 2010. However, activities were discontinued at the Bothell facility during the third quarter of 2005 and we are exploring options for the future of this facility.

Item 3. Legal Proceedings

From time to time, we may be involved in routine litigation incidental to the conduct of our business. As of December 31, 2006, we were not a party to any material legal proceedings.

Item 4. Submission of Matters to a Vote of Security Holders

No matters were submitted to a vote of the shareholders during the fourth quarter of 2006.

Table of Contents

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Price Range of Common Stock

Our common stock began trading March 16, 2004 and is traded on the Nasdaq Global Market. As of March 27, 2006, in connection with the name change from Xcyte Therapies, Inc. to Cyclacel Pharmaceuticals, Inc., we changed the symbol under which our common stock trades to 'CYCC' (previously 'XCYT'). Our preferred stock currently trades on the Nasdaq Capital Market under the symbol 'CYCCP'. The following table summarizes, for the periods indicated, the high and low sales prices for the common stock of Xcyte Therapies, Inc. (prior to March 27, 2006) and of Cyclacel Pharmaceuticals, Inc. after March 27, 2006), as reported by the Nasdaq Global Market, as adjusted to reflect the effect of a 1-for-10 reverse split of our common stock on March 27, 2006:

	High	Low
2006		
Quarter ended March 31, 2006	$ 8.70	$ 5.60
Quarter ended June 30, 2006	$ 8.30	$ 5.50
Quarter ended September 30, 2006	$ 6.91	$ 4.35
Quarter ended December 31, 2006	$ 7.95	$ 4.31
2005		
Quarter ended March 31, 2005	$ 29.20	$ 12.20

Quarter ended June 30, 2005	$ 14.50	$ 5.70
Quarter ended September 30, 2005	$ 7.90	$ 4.50
Quarter ended December 31, 2005	$ 7.50	$ 2.50

Holders of Common Stock

On March 15, 2007 we had approximately 120 registered holders of record of our common stock. On March 15, 2007, the closing sale price of our common stock as reported on the Nasdaq Global Market was $7.99 per share.

Dividends

We have never declared or paid any cash dividends on our common stock and do not currently anticipate declaring or paying any cash dividends on our outstanding shares of common stock in the foreseeable future. We are, however, required to make quarterly dividend payments on our convertible preferred stock. Our ability to pay dividends on our common stock may be limited if we fail to pay accrued dividends on our convertible preferred stock. Except for dividends we are paying on the convertible preferred stock, we currently intend to retain all of our future earnings, if any, to finance operations. Any future determination relating to our dividend policy will be made at the discretion of our board of directors and will depend on a number of factors, including future earnings, capital requirements, financial conditions, future prospects, contractual restrictions and other factors that our board of directors may deem relevant. Pursuant to the terms of our outstanding preferred stock, we currently pay dividends to the holders of our preferred stock.

Recent sales of unregistered securities

None.

Securities Authorised for Issuance Under Equity Compensation Plans

The information called for by this item is incorporated by reference from our definitive proxy statement which will be filed with the SEC within 120 days after the end of 2006 fiscal year pursuant to regulation 14A for our annual meeting to be held on May 21, 2007.

Table of Contents

Item 6. Selected Financial Data

This section presents our historical financial data. The statement of operations data for the years ended December 31, 2004, 2005 and 2006 and for the period from August 13, 1996 (inception) to December 31, 2006 and the balance sheet data as of December 31, 2005 and 2006 have been derived from our audited financial statements included elsewhere in this Form 10-K. The statement of operations data for the year ended March 31, 2003 and nine months ended December 31, 2003 and the balance sheet data as of March 31, 2003, and December 31, 2003 and 2004 have been derived from our audited financial statements that are not included in this Form 10-K. Historical results are not necessarily indicative of future results.

The information contained in the following tables should be read in conjunction with ‘Management’s Discussion and Analysis of Financial Condition and Results of Operations’ and the financial statements included in this Form 10-K.

	Year Ended March 31, 2003	Nine Months Ended December 31, 2003	Years ended December 31, 2004	2005	2006	Period from August 13, 1996 (inception) to December 31, 2006
			(in thousands, except share and per share data)			
Consolidated Statements of Operations:						
Revenues:						
Collaboration and research and development income	$ 1,250	$ 8	$ 102	$ 245	$ 231	$ 2,990
Grant income	941	504	823	111	156	3,477
	2,191	512	925	356	387	6,467
Operating expenses:						
Research and development	(20,091)	(13,258)	(20,332)	(15,841)	(21,205)	(121,975)
General and administrative	(2,597)	(2,142)	(3,554)	(5,290)	(12,319)	(35,953)
Other restructuring costs	—	—	—	—	(225)	(225)
Total operating expenses	(22,688)	(15,400)	(23,886)	(21,131)	(33,749)	(158,153)
Operating loss	(20,497)	(14,888)	(22,961)	(20,775)	(33,362)	(151,686)
Interest and other income (expense)	558	(1,575)	(2,237)	827	1,859	926
Loss before taxes	(19,939)	(16,463)	(25,198)	(19,948)	(31,503)	(150,760)
Income tax benefit	4,397	1,486	2,456	1,900	2,245	12,484
Net loss	(15,542)	(14,977)	(22,742)	(18,048)	(29,258)	(138,276)
Dividends on preferred shares	(4,654)	(4,425)	(11,053)	(11,876)	(2,827)	(38,123)
Net loss applicable to ordinary shareholders	$ (20,196)	$ (19,402)	$ (33,795)	$ (29,924)	$ (32,085)	$(176,399)
Net loss per share – basic and diluted	$ (22.01)	$ (11.31)	$ (5.10)	$ (4.50)	$ (2.40)	
Weighted average shares used to compute basic and diluted earnings per share	917,555	1,715,807	6,627,831	6,656,732	13,390,933	

Table of Contents

	As of March 31, 2003	As of December 31, 2003	2004	2005	2006
			(in thousands)		
Consolidated Balance Sheet Data:					
Cash and cash equivalents	$ 16,558	$ 4,335	$ 7,766	$ 3,117	$ 44,238
Short-term investments	1,575	29,345	15,152	10,690	9,764
Working capital	17,948	34,383	20,909	2,152	50,244
Total assets	26,881	42,800	31,176	19,071	63,276
Long-term debt, net of current portion	(184)	(495)	(368)	(78)	(1,436)
Preferred ordinary ‘C’ shares	(53,851)	—	—	—	—

Total stockholders' equity (deficit)	(32,147)	37,648	23,953	4,119	53,919

In connection with the stock purchase agreement Cyclacel Limited was considered to be the acquiring company for accounting purposes. Accordingly, the assets and liabilities of Xcyte were recorded, as of the date of the business combination, at their respective fair values and added to those of Cyclacel Limited. The results of the operations and balance sheet data for 2006 reflect the results of the combined companies from March 28, 2006 through December 31, 2006. Additionally, the historical results of operations and balance sheet data shown for comparative purposes in this Form 10-K reflect those of Cyclacel Limited prior to the reverse merger.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This report contains certain statements that may be deemed 'forward-looking statements' within the meaning of United States securities laws. All statements, other than statements of historical fact, that address activities, events or developments that we intend, expect, project, believe or anticipate will or may occur in the future are forward-looking statements. Such statements are based upon certain assumptions and assessments made by our management in light of their experience and their perception of historical trends, current conditions, expected future developments and other factors they believe to be appropriate. Factors that could cause results to differ materially from those projected or implied in the forward looking statements are set forth in this Annual Report on Form 10-K for the year ended December 31, 2006 under the caption 'Item 1A — Risk factors'.

We encourage you to read those descriptions carefully. We caution you not to place undue reliance on the forward-looking statements contained in this report. These statements, like all statements in this report, speak only as of the date of this report (unless an earlier date is indicated) and we undertake no obligation to update or revise the statements except as required by law. Such forward-looking statements are not guarantees of future performance and actual results will likely differ, perhaps materially, from those suggested by such forward-looking statements.

Overview

We are a development-stage biopharmaceutical company dedicated to the discovery, development and eventual commercialization of novel, mechanism-targeted drugs to treat human cancers and other serious disorders. Our core area of expertise is in cell cycle biology, or the processes by which cells divide and multiply. We focus primarily on the discovery and development of orally available anticancer agents that target the cell cycle with the aim of slowing the progression or shrinking the size of tumors, and enhancing quality of life and improving survival rates of cancer patients. We are generating several families of anticancer drugs that act on the cell cycle including Cyclin Dependent kinase (CDK) and Aurora kinase (AK) inhibitors. Although a number of pharmaceutical and biotechnology companies are currently attempting to develop CDK inhibitor drugs, we believe that our lead drug candidate, seliciclib, is the only orally available CDK inhibitor drug candidate currently in Phase IIb trials.

We are advancing three of our anticancer drug candidates, seliciclib, sapacitabine and CYC116 through in-house research and development activities. We have worldwide rights to commercialize

seliciclib, sapacitabine and CYC116 and our business strategy is to enter into selective partnership arrangements with these programs. We are also progressing further novel drug series, principally for cancer, which are at earlier stages. Taken together, our pipeline covers all four phases of the cell cycle, which we believe will improve the chances of successfully developing and commercializing novel drugs that work on their own or in combination with approved conventional chemotherapies or with other targeted drugs to treat human cancers.

Our corporate headquarters is located in Berkeley Heights, New Jersey, with our main research facility located in Dundee, Scotland, and a second research facility located in Cambridge, England.

From our inception in 1996 through December 31, 2006, we have devoted substantially all our efforts and resources to our research and development activities. We have incurred significant net losses since inception. As of December 31, 2006, our accumulated deficit during the development stage was $138.3 million. We expect to continue incurring substantial losses for the next several years as we continue to develop our clinical, pre-clinical and other drugs currently in development. Our operating expenses comprise research and development expenses and general and administrative expenses.

To date, we have not generated any product revenue but have financed our operations and internal growth through private placements, licensing revenue, interest on investments, government grants and research and development tax credits. We have received proceeds from the issuances of equity interests of $133.5 million, net of issuance costs, from inception through December 31, 2006 which includes $42.6 million raised through the private placement of common stock and warrants in the second quarter of 2006. Our revenue has consisted of collaboration and grant revenue. We have recognized revenues from inception through December 31, 2006 of $6.5 million of which $3.0 million is derived from fees under collaborative agreements and $3.5 million of grant revenue from various United Kingdom government grant awards. We have not generated any revenue from sales of commercial products and do not expect to generate any product revenue for the foreseeable future. We have also recognized amounts receivable from H.M. Revenue & Customs of $12.5 million for research and development tax credits since inception.

Results of Operations

As explained in the Notes to Consolidated Financial Statements — Basis of Presentation, in connection with the stock purchase agreement, Cyclacel Limited was considered to be the acquiring company for accounting purposes. Accordingly, the assets and liabilities of Xcyte were recorded, as of March 27, 2006, at their respective fair values and added to those of Cyclacel Limited. The results of operations and balance sheet data for 2006 reflect the results of the combined companies from March 28, 2006 through December 31, 2006. Additionally, the historical results of operations and balance sheet data shown for comparative purposes in this Form 10-K reflect those of Cyclacel Limited prior to the reverse acquisition.

Years ended December 31, 2005 and 2006 compared to years ended December 31, 2004 and 2005, respectively

Revenues

The following table summarizes the components of our revenues for the years December 31, 2004, 2005 and 2006:

Years ended December 31,			$ Differences		% Differences	
			2004 to	2005 to	2004 to	2005 to
2004	2005	2006	2005	2006	2005	2006
		(in thousands)				
$ 102	$ 245	$ 231	$ 143	$ (14)	140.2%	(5.7)%

Collaboration and research and development revenue							
Grant revenue	823	111	156	(712)	45	(86.5)%	40.5%
Total revenue	$ 925	$ 356	$ 387	$ (569)	$ 31	(61.5)%	8.7%

Collaboration and research and development revenue is derived from several agreements under which the Company provides compounds for evaluation for an agreed consideration.

Table of Contents

Grant revenue is recognized as we incur and pay for qualifying costs and services under the applicable grant. Grant revenue is primarily derived from various United Kingdom government grant awards. During the years ended December 31, 2005 and 2006 two of those grants were fully paid.

Research and development expenses

To date, we have focused on drug discovery and development programs, with particular emphasis on orally available anticancer agents. Research and development expense represents costs incurred to discover and develop novel small molecule therapeutics, including clinical trial costs for seliciclib and sapacitabine, to advance product candidates toward clinical trials, to develop in-house research and preclinical study capabilities and to advance our biomarker program and technology platforms. We expense all research and development costs as they are incurred. Research and development expenses primarily include:

- payroll and personnel-related expenses, including consultants and contract research;
- clinical trial and regulatory-related costs;
- preclinical studies;
- screening and identification of drug candidates;
- laboratory supplies and materials;
- technology license costs;
- rent and facility expenses for our laboratories; and
- scientific consulting fees.

The following table provides information with respect to our research and development expenditure for the years ended December 31, 2004, 2005 and 2006:

	Years ended			$ Differences		% Differences	
	2004	2005	2006	2004 to 2005	2005 to 2006	2004 to 2005	2005 to 2006
				(in thousands)			
Seliciclib	$ 6,626	$ 4,777	$ 3,126	$ (1,849)	$ (1,651)	(27.9)%	(34.6)%
Sapacitabine	2,069	2,236	1,841	167	(395)	8.1%	(17.7)%
CYC116	2,321	5,397	6,712	3,076	1,315	132.5%	24.4%
Other costs related to research and development programs,	9,316	3,431	9,526	(5,885)	6,095	(63.2)%	177.6%

management and exploratory research							
Total research and development expenses	$ 20,332	$ 15,841	$ 21,205	$ (4,491)	$ 5,364	(22.1)%	33..9%

Research and development expenses represented 85.1%, 75.0% and 62.8% of our operating expenses for the years ended December 31, 2004, 2005 and 2006.

Fiscal 2006 as compared to fiscal 2005. Research and development costs increased 33.9% or $5.4 million from $15.8 million in the year ended December 31, 2005 to $21.2 million in the year ended December 31, 2006. The overall increase primarily relates to an increase in the charge for stock-based compensation of $6.5 million offset by the effects of the phasing of our clinical trials with the completion stages of Phase IIa clinical trials of seliciclib in 2005 followed by a period of reduced spending prior to the start of the Phase IIb trial in the second quarter of 2006. Expenditure increased gradually as our efforts focused on initiating the recruited sites for the Phase IIb trials during the second half of 2006 together with an increase in research and development expenditure on CYC116 as activities focused on IND-directed studies on this program culminating in the filing of the IND as scheduled in December 2006.

Fiscal 2005 as compared to fiscal 2004. Research and development costs decreased 22.1% or $4.5 million from $20.3 million in the year ended December 31, 2004 to $15.8 million in the year ended

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Table of Contents

December 31, 2005. The decrease reflects the completion of Phase IIa clinical trials of Seliciclib in 2005 and a deliberate strategy to reduce expenses and focus resources on oncology development programs during fiscal 2005.

Stock-based compensation attributable to research and development was an expense of $0.3 million, a credit of $0.3 million and an expense of $6.2 million for the years ended December 31, 2004, 2005 and 2006, respectively. Stock-based compensation is discussed below in greater detail.

The future

We plan to increase our investment in our research and development programs to further enhance our clinical and regulatory capabilities to allow us to advance the development of our drug candidates.

General and administrative expenses

General and administrative expenses include costs for administrative personnel, legal and other professional expenses and general corporate expenses. The following table summarizes the general and administrative expenses for the years ended December 31, 2004, 2005 and 2006:

	Years ended			$ Differences		% Differences	
				2004 to	2005 to	2004 to	2005 to
	2004	2005	2006	2005	2006	2005	2006
				(in thousands)			

Total general and administrative expenses	$ 3,554	$ 5,290	$ 12,319	$ 1,736	$ 7,029	48.9%	132.9%

Total general and administrative expenses represented 14.9%, 25.0% and 36.5% of our operating expenses for the years ended December 31, 2004, 2005 and 2006, respectively.

Fiscal 2006 as compared to fiscal 2005. General and administrative expenditure increased 132.9% or $7.0 million from $5.3 million in the year ended December 31, 2005 to $12.3 million in the year ended December 31, 2006. The increase arises primarily from the new combined business entity and our increased costs of operating as a public company and increased compensation and benefit expenses. The charge for stock-based compensation increased $3.4 mllion in the year ended December 31, 2006 compared to the same period in 2005. Salary and benefit expense increased by $1.4 million in the year ended December 31, 2006 compared with the same period in 2005. This increase was due primarily to the incorporation of payroll costs of remaining support staff of Xcyte as of March 28, 2006, increased bonus payments and United Kingdom payroll taxes incurred in connection with the issue of Group Preferred D shares to certain directors and officers in March 2006 prior to the Stock Purchase. Regulatory, corporate and advisors costs together with insurances have increased $1.2 million, of which approximately $0.2 million relates to compliance costs of Section 404 of the Sarbanes Oxley Act, in the year ended December 31, 2006 compared with the same period in 2005. Rental and maintenance of the Seattle office and Bothell manufacturing facilities together with our corporate head quarters in New Jersey have given rise to $0.7 million of additional costs in the year ended December 31, 2006. There were no comparable expenses recognized in the year ended December 31, 2005.

Fiscal 2005 as compared to fiscal 2004. General and administrative expenditure increased 48.9% or $1.7 million from $3.6 million in the year ended December 31, 2004 to $5.3 million in the year ended December 31, 2005. This increase was primarily due to increased intellectual property maintenance fees and other related costs of $0.5 million and costs related to financing activities of $0.9 million.

Stock-based compensation related to general and administrative expense for the years ended December 31, 2004, 2005 and 2006 was Nil, Nil and $3.4 million, respectively. Stock-based compensation is discussed below in greater detail.

The future

As a public company, we operate in an increasingly demanding regulatory environment that requires us to comply with the Sarbanes-Oxley Act of 2002 and the related rules and regulations of the Securities and Exchange Commission, or SEC, and the Nasdaq Global Market for our common stock and Nasdaq

Table of Contents

Capital Market for our preferred stock, including those related to expanded disclosures, accelerated reporting requirements and more complex accounting rules. We expect that our general and administrative expenses will continue to increase in subsequent periods due to these requirements.

Stock-based compensation expenses

We adopted SFAS 123R on January 1, 2006. Previously we recognized stock-based compensation in accordance with the provisions of APB No. 25. Prior period figures have not been restated and therefore are not comparable to the current year presentation. Stock-based compensation expenses includes charges/(credits) related to options issued to

employees, directors and non-employees.

The following table summarizes the components of our stock-based compensation for the years ended December 31, 2004, 2005 and 2006:

	Years ended			$ Differences		% Differences	
	2004	2005	2006	2004 to 2005	2005 to 2006	2004 to 2005	2005 to 2006
	(in thousands)						
Research and development related	$ 291	$ (295)	$ 6,230	$ (586)	$ 6,525	(201.4)%	2,211.9%
General and administrative related	(12)	(39)	3,370	(27)	3,409	225.0%	8,741.0%
Total stock based compensation	$ 279	$ (334)	$ 9,600	$ (613)	$ 9,934	(219.7)%	2,974.3%

For the years ended December 31 2004 and 2005 we recognized a stock-based compensation charge of $0.3 million and a credit of $0.3 million, respectively. The credits recognized arose from an up-date of the market value of the underlying common stock under APB No. 25.

As required by the provisions of SFAS 123R we recorded a stock-based compensation charge of $9.6 million in the year ended December 31, 2006. The stock-based compensation charge is comprised of (i) $5.2 million related to restricted stock granted to certain employees and directors (ii) $1.8 million due to the acceleration of vesting of options due to the Stock Purchase and (iii) $2.6 million relating to the options granted in the second, third and fourth quarters of 2006 under the 2006 Plan. In the second quarter of 2006, we granted 829,079 stock options under the 2006 Plans, of which two-thirds were fully vested on grant. The remaining unvested options will become fully vested by June 13, 2007. In the third quarter of 2006, we granted 16,667 stock options under the 2006 Plans which vest rateably over three years to August 1, 2009. In the fourth quarter of 2006 we granted 488,333 stock options under the 2006 Plans of which 8,333 vest rateably over three years to October 31, 2009, 40,000 vest rateably over four years to October 31, 2010, 390,000 of which one-quarter vest on the first anniversary of date of grant with the balance vesting rateably over three years to December 21, 2010, and 50,000 which will become fully vested on December 31, 2007, approximately 12 months following the date of grant.

The future

We may from time to time continue to grant options or other stock-based awards, to our employees, directors and, as appropriate, to non-employee service providers, which will result in an expense. In addition, previously-granted options will continue to vest in accordance with their terms. The total fair value of all options granted under the 2006 Plans is $5,732,000. In respect of these options, $3,132,000 of compensation expense has not been recognized at December 31, 2006.

Restructuring charge

The following table summarizes the restructuring charges for years ended December 31, 2004, 2005 and 2006:

	Years ended			$ Differences	% Differences
	2004	2005	2006		

				2004 to 2005	2005 to 2006	2004 to 2005	2005 to 2006
			(in thousands)				
Total restructuring charge	$ —	$ —	$ 225	$ —	$ 225	0.0%	100.0%

43

Table of Contents

In March 2006, the Company assumed an accrued restructuring liability in relation to the Bothell manufacturing facility, calculated as the net present value of the difference between the remaining lease payments due less the estimate of net sublease income and expenses. In September 2006, the Company entered into an Exclusive Subleasing Agency Agreement in an attempt to achieve the successful sublet of the facility. As a result of the agreement, we recorded an additional provision in the third quarter of 2006 of $225,000 in recognition of commissions payable upon successful conclusion of a sublease agreement. No such restructuring expense was recognized in the years ended December 31, 2004 and 2005.

Future

As at December 31, 2006, the restructuring liability associated with exiting the Bothell facility was $2.3 million accounting for the estimated fair value of the remaining lease payments, net of estimated sub-lease income. The restructuring liability is subject to a variety of assumptions and estimates. We review these assumptions and estimates on a quarterly basis and will adjust the accrual if necessary. These changes can be material.

Other income (expense)

Other income (expense) is comprised of costs associated with an aborted IPO in 2004, the change in valuation of the derivative, interest income and interest expense. The following table summarizes the other income (expense) for years ended December 31, 2004, 2005 and 2006:

	Years ended			$ Differences		% Differences	
	2004	2005	2006	2004 to 2005	2005 to 2006	2004 to 2005	2005 to 2006
			(in thousands)				
Costs associated with aborted 2004 IPO	$ (3,550)	$ —	$ —	$ 3,550	$ —	100.0%	—
Change in valuation of derivative	—	—	(215)	—	(215)	—	(100.0)%
Interest income	1,425	887	2,328	(538)	1,441	(37.8)%	162.5%
Interest expense	(112)	(60)	(254)	52	(194)	46.4%	(323.3)%
Total other income (expense)	$ (2,237)	$ 827	$ 1,859	$ 3,064	$ 1,032	137.0%	124.8%

The change in the derivative value of $215,000 in 2006 is associated with the dividend make-whole payment on our outstanding convertible exchangeable preferred stock. No such derivative valuation expense was recognized in the years ended December 31, 2004 and 2005.

Fiscal 2006 as compared to fiscal 2005. The increase in interest income from $0.9 million in 2005 to $2.3 million in 2006 is primarily attributable to higher average balance of cash and cash equivalents and short-term investments in 2006 following receipt of $42.6 million being the net proceeds of our private placement in the second quarter and the $21.1 million of cash and cash equivalents and short-term investments assumed on the Stock Purchase. The increase in interest expense to $0.3 million in 2006 as compared to $60,000 in 2005 resulted primarily from accretion expense associated with the Bothell lease restructuring provision. During the year ended December 31, 2006 we recognized accretion expense of $0.2 million. No such accretion expense was recognized in the years ended December 31, 2004 and 2005.

Fiscal 2005 as compared to fiscal 2004. The decrease in interest income from $1.4 million in 2004 to $0.9 million in 2005 is primarily attributable to reducing average balance of cash and cash equivalents and short-term investments in 2005.

The future

The valuation of the dividend make-whole payment will continue to be re-measured at the end of each reporting period. The valuation of the derivative is dependent upon many factors, including estimated market volatility, and may fluctuate significantly, which may have a significant impact on our statement of operations.

Table of Contents

A further accretion expense of approximately $0.3 million associated with the Bothell lease restructuring charge will be recognized over the remaining life of the lease through November 2010.

Income tax benefit

Credit is taken for research and development tax credits, which are claimed from the United Kingdom's taxation and customs authority, in respect of qualifying research and development costs incurred.

The following table summarizes research and development tax credits for the years ended December 31, 2004, 2005 and 2006:

	Years ended			$ Differences		% Differences	
				2004 to	2005 to	2004 to	2005 to
	2004	2005	2006	2005	2006	2005	2006
		(in thousands)					
Total income tax benefit	$ 2,456	$ 1,900	$ 2,245	$ (556)	$ 345	(22.6)%	18.2%

Fiscal 2006 as compared to fiscal 2005. Research and development tax credits recoverable increased 18.2% or $0.3 million from $1.9 million in 2005 to $2.2 million in 2006. The level of tax credits recoverable is linked directly to qualifying research and development expenditure incurred in any one year but restricted to income taxes paid by the Company in that same year. This increase was a reflection of the increased income taxes available to recover from the taxes paid in connection with the issue of Group Preferred D shares to certain directors and officers in March 2006, prior to the Stock Purchase.

Fiscal 2005 as compared to fiscal 2004. Research and development tax credits recoverable fell 22.6% or $0.6 million from $2.5 million in 2004 to $1.9 million in 2005. This decrease was a reflection of a reduced level of qualifying research and development expenditure in the year ended December 31, 2005 combined with a decrease in income taxes available for recovery.

Future

We expect to continue to be eligible to receive United Kingdom research and development tax credits for the foreseeable future and will elect to do so.

Liquidity and Capital Resources

The following is a summary of our key liquidity measures as December 31, 2005 and 2006:

	December 31, 2005	December 31, 2006	$ Difference	% Difference
		(in thousands)		
Cash and cash equivalents	$ 3,117	$ 44,238	$ 41,121	1,319.3%
Short-term investments, available for sale	10,690	9,764	(926)	(8.7)%
Total cash and cash equivalents and short-term investments, available for sale	$ 13,807	$ 54,002	$ 40,195	291.1%
Current assets	$ 17,026	$ 58,165	$ 41,139	241.6%
Current liabilities	14,874	7,921	(6,953)	(46.8)%
Working capital	$ 2,152	$ 50,244	$ 48,092	2,234.8%

Since our inception, we have not generated any significant product revenue and have relied primarily on the proceeds from sales of equity and preferred securities to finance our operations and internal growth. Additional funding has come through interest on investments, licensing revenue, government grants and research and development tax credits. We have incurred significant losses since our inception. As of December 31, 2006, we had an accumulated deficit of $138.3 million.

We believe that existing funds together with cash generated from operations and financing are sufficient to satisfy our planned working capital, capital expenditures, debt service and other financial commitments through to at least the next 12 months.

Table of Contents

At December 31, 2005, we had cash and cash equivalents and short-term investments of $13.8 million as compared with $54.0 million at December 31, 2006. This higher balance at December 31, 2006 was primarily due to the receipt of net proceeds of $42.6 million from the private placement, $21.1 million of cash and cash equivalents and short-term investments assumed on completion of the Stock Purchase and $9.2 million received from our former parent company, described below.

On July 28, 2005, Cyclacel Group plc ('Group') signed a convertible Loan Note Instrument constituting convertible unsecured loan notes. On July, 28, 2005, it entered into a Facility Agreement with Scottish Enterprise, as lender, whereby Scottish Enterprise subscribed for £5 million (approximately $9 million) of the convertible loan notes. Upon the completion of the Stock Purchase, the convertible loan notes held by Scottish Enterprise converted into 1,231,527 preferred D shares in satisfaction of all amounts owed by Group under the convertible loan notes. The number of preferred D shares that Scottish Enterprise received was calculated by dividing the principal amount outstanding under the loan note by £4.06. Scottish Enterprise retains the ability it had under the Facility Agreement to receive a cash payment should the research operations in Scotland be significantly reduced. However, Cyclacel has guaranteed the amount potentially due to Scottish Enterprise which would be calculated as a maximum of approximately $9 million (£5 million) less the market value of the shares held (or would have held in the event they dispose of any shares) by Scottish Enterprise at the time of any significant reduction in research facilities during the period ending on July 28, 2010.

Cyclacel was also a party to a long-term debt instrument, a government loan of $441,000 that accrued interest at 5% per annum, and this loan was wholly repaid in November 2005.

The following is a summary of our contractual obligations and other commitments relating to our facilities, equipment leases and purchases as at December 31, 2006, and the effect such obligations could have on our liquidity:

	Payments due by period				
	Total	Less than 1 year	1-3 years	4-5 years	After 5 years
			(in thousands)		
Capital lease obligations	$ 89	$ 89	$ —	$ —	$ —
Operating lease obligations	9,596	2,140	4,328	2,617	511
Purchase obligations	1,215	1,215	—	—	—
Total	$ 10,900	$ 3,444	$ 4,328	$ 2,617	$ 511

We also currently have a number of contractual arrangements with our partners under which milestone payments totaling $23.4 million would be payable subject to achievement of all the specific contractual milestones and our decision to continue with these projects. Under these contractual arrangements, we make annual payments that do not and will not exceed $0.1 million.

Cash provided by (used in) operating, investing and financing activities for the years ended December 31, 2004, 2005 and 2006, is summarized as follows:

	Year ended December 31,		
	2004	2005	2006
		(in thousands)	
Net cash used in operating activities	$ (19,633)	$ (15,141)	$ (20,172)
Net cash provided by investing activities	$ 15,617	$ 2,745	$ 3,911
Net cash provided by financing activities	$ 6,937	$ 8,354	$ 57,400

Fiscal 2006 as compared to fiscal 2005. Net cash used in operating activities increased $5.1 million, from $15.1 million in 2005 to $20.2 million in 2006. Net cash used in operating activities during 2006 of $20.2 million resulted primarily from our net loss of $29.3 million. Net cash provided by investing activities increased $1.2 million,

from $2.7 million in 2005 to $3.9 million in 2006. Net cash provided by investing activities resulted primarily from the sale and maturity of short-term investments, the proceeds of which were used to fund our operating activities. Net cash provided by financing activities increased

Table of Contents

$49.1 million, from $8.3 million in 2005 to $57.4 million in 2006. During 2006 the net cash provided by financing activities related primarily to proceeds received from the private placement of $42.6 million and the $17.9 million of cash and cash equivalents assumed on the Stock Purchase offset by payment of our preferred stock dividend of $0.9 million, costs associated with the Stock Purchase of $2.0 million and the payment of capital lease obligations of $0.3 million.

Fiscal 2005 as compared to fiscal 2004. Net cash used in operating activities decreased $4.5 million, from $19.6 million in 2004 to $15.1 million in 2005. Net cash used in operating activities during 2005 of $15.1 million resulted primarily from our net loss of $18.0 million. Net cash provided by investing activities decreased $12.9 million, from $15.6 million in 2004 to $2.7 million in 2005. Net cash provided by investing activities resulted primarily from the sale and maturity of our short-term investments, the proceeds of which were used to fund our operating activities. Net cash provided by financing activities increased $1.5 million, from $6.9 million in 2004 to $8.4 million in 2005.

During the year ended December 31, 2005, the net cash provided by financing activities related to $9.2 million received from our former parent company, described above, offset by payment of capital lease obligations.

Capital spending is vital to our research and development initiatives and to maintain our operational capabilities. During the years ended December 31, 2005 and 2006 we used cash of $0.3 million in 2005 to develop our research facilities in Cambridge, England, and $0.7 million in 2006 to refurbish our new corporate offices in New Jersey and to acquire smaller, but key items, of research and development equipment and replacement items essential to support our information technology function.

Operating Capital and Capital Expenditure Requirements

We expect to continue to incur substantial operating losses in the future. We will not receive any product revenue until a product candidate has been approved by the FDA or similar regulatory agencies in other countries and successfully commercialized. We currently anticipate that our cash, cash equivalents, marketable securities and proceeds from the private placement will be sufficient to fund our operations at least through the next 12 months. However, we will need to raise substantial additional funds to continue our operations beyond such time. We cannot be certain that any of our programs will be successful or that we will be able to raise sufficient funds to complete the development and commercialize any of our product candidates currently in development, should they succeed. Additionally, we plan to continue to evaluate in-licensing and acquisition opportunities to gain access to new drugs or drug targets that would fit with our strategy. Any such transaction would likely increase our funding needs in the future.

Our future funding requirements will depend on many factors, including but not limited to:

- the rate of progress and cost of our clinical trials, preclinical studies and other discovery and research and development activities;

- the costs associated with establishing manufacturing and commercialization capabilities;
- the costs of acquiring or investing in businesses, product candidates and technologies;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;
- the costs and timing of seeking and obtaining FDA and other regulatory approvals;
- the effect of competing technological and market developments; and
- the economic and other terms and timing of any collaboration, licensing or other arrangements into which we may enter.

Until we can generate a sufficient amount of product revenue to finance our cash requirements, which we may never do, we expect to finance future cash needs primarily through public or private equity offerings, debt financings or strategic collaborations. We do not know whether additional funding will be available on acceptable terms, or at all. If we are not able to secure additional funding when needed, we

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Table of Contents

may have to delay, reduce the scope of or eliminate one or more of our clinical trials or research and development programs. In addition, we may have to partner one or more of our product candidate programs at an earlier stage of development, which would lower the economic value of those programs to us.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

We are exposed to market risk related to fluctuations in interest rates and in foreign currency exchange rates.

Interest Rate Risk

Our short-term investments as of December 31, 2006 consisted of $1.8 million in corporate bonds and $7.9 million in federal agency obligations with contractual maturities of one year or less. Due to the short-term nature of our investments, we believe that our exposure to market interest rate fluctuations is minimal. The corporate bonds in which we invest are rated ‘A‘ or better by both Moody’s and Standard and Poor’s. Our cash and cash equivalents are held primarily in highly liquid money market accounts. A hypothetical 10% change in short-term interest rates from those in effect at December 31, 2006 would not have a significant impact on our financial position or our expected results of operations. We do not currently hold any derivative financial instruments with interest rate risk.

Foreign Currency Risk

We are exposed to foreign currency rate fluctuations related to the operation of our subsidiary in the United Kingdom. At the end of each reporting period, income and expenses of the subsidiary are remeasured into U.S. dollars using the average currency rate in effect for the period and assets and liabilities are remeasured into U.S. dollars using either historical rates or the exchange rate in effect at the end of the period. We currently do not engage in foreign currency hedging; however, we have entered into certain contracts denominated in foreign currencies and, therefore, we are subject to currency exchange risks. As of December 31, 2006 differences on foreign currency translation of $416,000 are shown as a movement in other comprehensive income. In the year ended December 31, 2006 exchange rate differences of $43,000 were charged in the statements of operations.

Derivatives Valuation Risk

The Company's convertible exchangeable preferred stock issued in November 2004 remained in place following completion of the Stock Purchase. The terms of the convertible preferred stock include a dividend make-whole payment feature. This feature is considered to be an embedded derivative and was valued on the balance sheet at $1.1 million at December 31, 2006. As the fair value of this derivative may fluctuate significantly from period to period, the resulting change in valuation may have a significant impact on our results of operations. Please refer to note 12 of the notes to the consolidated financial statements for further details.

Item 8. Financial Statements and Supplementary Data

INDEX TO CYCLACEL PHARMACEUTICALS, INC. FINANCIAL STATEMENTS

Table of Contents

CYCLACEL PHARMACEUTICALS, INC.
(A Development Stage Company)

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Shareholders
Cyclacel Pharmaceuticals, Inc.

We have audited the accompanying consolidated balance sheets of Cyclacel Pharmaceuticals, Inc. (a development stage company) as of December 31, 2006 and 2005, and the related consolidated statements of operations, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2006 and the period from August 13, 1996 (inception) to December 31, 2006. These financial statements are the responsibility of the

Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Cyclacel Pharmaceuticals, Inc.(a development stage company) at December 31, 2006 and 2005, and the consolidated results of its operations and its consolidated cash flows for each of the three years in the period ended December 31, 2006 and for the period from August 13, 1996 (inception) to December 31, 2006, in conformity with U.S. generally accepted accounting principles.

As discussed in Note 2 to the consolidated financial statements, effective January 1, 2006, the Company adopted the provisions of Statement of Financial Accounting Standards No. 123R 'Shared-Based Payment'.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the effectiveness of Cyclacel Pharmaceuticals, Inc.'s internal control over financial reporting as of December 31, 2006, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated March 16, 2007 expressed an unqualified opinion thereon.

/s/ ERNST & YOUNG LLP

London, England

March 16, 2007

50

Table of Contents

CYCLACEL PHARMACEUTICALS, INC.
(A Development Stage Company)

CONSOLIDATED BALANCE SHEETS

	December 31,	
	2005	2006
	$000	$000
ASSETS		
Current assets:		
Cash and cash equivalents	3,117	44,238
Short-term investments	10,690	9,764
Prepaid expenses and other current assets	3,219	4,163

Total current assets	17,026	58,165
Property, plant and equipment (net)	2,045	2,121
Deposits and other assets	—	241
Goodwill	—	2,749
Total assets	19,071	63,276
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	2,159	2,175
Amounts due to Cyclacel Group plc	10,467	—
Accrued liabilities	1,869	3,324
Other current liabilities	128	290
Derivative liability	—	1,135
Current portion of other accrued restructuring charges	—	908
Current portion of equipment financing	251	89
Total current liabilities	14,874	7,921
Other accrued restructuring charges, net of current	—	1,436
Equipment financing, net of current	78	—
Total liabilities	14,952	9,357
Commitments and contingencies (Note 11)		
Stockholders' equity (deficit):		
Preferred stock, $0.001 par value; Nil and 5,000,000 shares authorized at December 31, 2005 and 2006, respectively; Nil and 2,046,813 shares issued and outstanding at December 31, 2005 and 2006, respectively. Aggregate preference in liquidation of $Nil and $20,673,000 at December 31, 2005 and 2006, respectively	—	2
Common stock, $0.001 par value; 100,000,000 shares authorized at December 31, 2005 and 2006, respectively; 6,656,732 and 16,157,953 shares issued and outstanding at December 31, 2005 and 2006, respectively	7	16
Additional paid in capital	116,088	194,714
Accumulated other comprehensive loss	(2,958)	(2,537)
Deficit accumulated during the development stage	(109,018	(138,276)
Total stockholders' equity	4,119	53,919
Total liabilities and stockholders' equity	19,071	63,276

See accompanying notes

Table of Contents

CYCLACEL PHARMACEUTICALS, INC.
(A Development Stage Company)

CONSOLIDATED STATEMENTS OF OPERATIONS

	Year ended December 31, 2004	Year ended December 31, 2005	Year ended December 31, 2006	Period from August 13, 1996 (inception) to December 31, 2006
	$000, except per share and share amounts			
Revenues:				
Collaboration and research and development revenue	102	245	231	2,990
Grant revenue	823	111	156	3,477
	925	356	387	6,467
Operating expenses:[1]				
Research and development	(20,332)	(15,841)	(21,205)	(121,975)
General and administrative	(3,554)	(5,290)	(12,319)	(35,953)
Other restructuring costs	—	—	(225)	(225)
Total operating expenses	(23,886)	(21,131)	(33,749)	(158,153)
Operating loss	(22,961)	(20,775)	(33,362)	(151,686)
Other income (expense):				
Costs associated with aborted 2004 IPO	(3,550)	—		