Cyclacel Pharmaceuticals, Inc.
Form 10-K
March 31, 2009

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

Form 10-K

(Mark One)

þ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2008

or

o **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934B**

Commission file number 00-50626

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

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

Securities registered under Section 12(b) of the Exchange Act:
None.

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

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 o No þ

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 þ No o

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 o.

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

Large accelerated filer o	Accelerated filer o	Non-accelerated filer o [Do not check if a smaller reporting company]	Smaller reporting company þ

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

The aggregate market value of the registrant s voting and non-voting common stock held by non-affiliates of the registrant (without admitting that any person whose shares are not included in such calculation is an affiliate) (based upon the closing sale price of $1.91 of such shares on The NASDAQ Global Market on June 30, 2008) was $19,224,097.

As of March 30, 2009, there were 20,433,129 shares of the registrant s common stock outstanding.

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 Definitive Proxy Statement relating to the 2009 Annual Meeting of Stockholders, which we will file with the SEC within 120 days after our December 31, 2008 fiscal year end.

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PART I

Item 1. *Business*

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

General

Cyclacel Pharmaceuticals, Inc. was incorporated in the state of Delaware in 1996 and is headquartered in Berkeley Heights, New Jersey with a research facility located in Dundee, Scotland. Cyclacel is a development-stage biopharmaceutical company dedicated to the discovery, development and commercialization of novel, mechanism-targeted drugs to treat human cancers and other serious disorders. Cyclacel s strategy is focused on leading edge therapeutic management of cancer patients based on a portfolio of three products marketed by its ALIGN Pharmaceuticals, LLC or ALIGN subsidiary and a clinical development pipeline. 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 property, raising capital and recruiting and training personnel.

Recent Developments

On February 6, 2009, we announced progress with a pivotal trial plan for sapacitabine, our oral nucleoside analogue, for the treatment of hematological malignancies. The announcement followed our meeting with the U.S. Food and Drug Administration or FDA. The pivotal trial plan consists of treating in an open-label, single arm study of approximately 100 patients with acute myeloid leukemia or AML or myelodysplastic syndromes or MDS on a dosing regimen to be selected from the currently ongoing randomized Phase 2 study of oral sapacitabine in elderly patients.

On January 13, 2009, we announced that the Company began treating patients in a Phase 2, open label, single arm, multicenter clinical trial of sapacitabine in patients with non-small cell lung cancer or NSCLC who have had one prior chemotherapy.

On October 9, 2008, we announced the completion of enrollment as per the protocol in the Phase 2 clinical trial of sapacitabine in elderly patients with AML. Final results are expected to be available during the second half of 2009.

On September 16, 2008, we announced a revision of our operating plan to concentrate our resources on the advancement of our lead drug, sapacitabine, while maintaining our core competency in drug discovery and cell cycle biology. The plan reduced the workforce across all locations by 25 people or approximately 30%. As part of the revised operating plan, we are closing our research facility in Cambridge, United Kingdom.

Corporate information

Our corporate headquarters are located at 200 Connell Drive, Suite 1500, Berkeley Heights, New Jersey, 07922, and our telephone number is 908-517-7330. This is also where our medical and regulatory functions are located. Our research facility is located in Dundee, Scotland which is also the center of our structure-based drug design, translational work and development programs.

Overview

We are a diversified biopharmaceutical business dedicated to the discovery, development and commercialization of novel, mechanism-targeted drugs to treat cancer and other serious disorders. Our strategy is focused on leading edge therapeutic management of cancer patients based on a portfolio of three medicines marketed by our ALIGN subsidiary and a clinical development pipeline. Our core area of expertise is in cell cycle biology, or the processes by which cells divide and multiply. We focus primarily on the 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 the quality of life and improving survival rates of cancer patients. We have been focusing on the cell

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cycle since our inception. We market directly in the United States Xclair® Cream for radiation dermatitis and Numoisyn® Liquid and Numoisyn® Lozenges for xerostomia.

As a result of the revised operating plan announced on September 16, 2008, we are focusing our clinical development priorities on:

Sapacitabine in AML in the elderly;

Sapacitabine in MDS;

Sapacitabine in cutaneous T-cell lymphoma or CTCL; and

Sapacitabine in NSCLC.

We may continue to fund certain additional programs pending the availability of clinical data, at which time we will determine the feasibility of pursuing advanced development including:

Seliciclib in nasopharyngeal cancer or NPC;

Seliciclib in NSCLC; and

CYC116 in patients with solid tumors.

We were founded 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. Our Chief Scientist, Professor David Glover, is a recognized leader in the biology of mitosis or cell division. Professor Glover 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 to build a diversified biopharmaceutical business focused in oncology, hematology and other therapeutic areas based on a portfolio of commercial products and a development pipeline of novel drug candidates.

We are advancing our three anticancer drug candidates, sapacitabine, seliciclib and CYC116, through in-house development activities. We are also progressing further novel drug series 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. For the years ended December 31, 2007 and 2008, research and development expenditures totaled approximately $19.6 million and $18.9 million, respectively.

We have executed our strategy through the following activities:

Advancing our research and development programs

Sapacitabine received orphan designation for AML & MDS from EU regulators;

Seliciclib APPRAISE Phase 2b NSCLC independent data review committee review of the first interim analysis data;

Sapacitabine expands Phase 2 trial in elderly AML patients to include patients with MDS;

Sapacitabine Phase 2 elderly AML trail completed enrollment;

Sapacitabine Phase 2 NSCLC trial commenced; and

Announced progress with a pivotal trial plan for sapacitabine in AML or MDS following a meeting with the FDA.

Managing our resources

Revised operating plan which resulted in an approximate 30% reduction in workforce, closure of our Cambridge research facility and a decrease in operating cost base of approximately $9.0 million.

Ended 2008 with approximately $25.7 million of cash and cash equivalents and short-term investments.

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Enhancing our skills base

Appointed Robert Sosnowski as Vice President, Sales and Marketing.

Named Nicholas Bacopoulos, Ph.D., to the Board of Directors.

Commercial products

On October 5, 2007, we acquired, through ALIGN, the exclusive rights to sell and distribute three products in the United States and Canada used primarily to manage the effects of radiation or chemotherapy in cancer patients: Xclair® Cream, Numoisyn® Liquid and Numoisyn® Lozenges. All three products are approved in the United States under FDA 510 (k) or medical device registrations. All three products were launched in the United States in January 2006.

Xclair® Cream

Xclair® is an aqueous cream containing sodium hyaluronate, or hyaluronic acid and glycyrrhetinic acid that is formulated to relieve symptoms associated with radiation dermatitis. Sodium hyaluronate is the key water-regulating substance in human skin. Sodium hyaluronate has high viscoelasticity and lubricity. When sodium hyaluronate solution is applied on the surface of skin, it forms an air permeable layer that keeps skin moist and smooth. Small molecular weight sodium hyaluronate can penetrate into the dermis where it combines with water to promote microcirculation, nutrient absorption, and metabolism. Glycyrrhetinic acid reduces inflammation and is believed to have immunomodulatory properties.

Numoisyn® Liquid

Numoisyn® Liquid is an oral solution used to replace natural saliva when salivary glands are damaged. The viscosity of Numoisyn® Liquid is similar to that of natural saliva. Linseed extract in Numoisyn® Liquid contains mucins that provide superior viscosity and reduced friction compared to water or carboxymethylcellulose or CMC solutions. Linseed extract significantly reduces the symptoms of dry mouth with increasing effect over time while Numoisyn® Liquid is used.

Numoisyn® Lozenges

Numoisyn® Lozenges dissolve slowly while moved around in the mouth. They contain sorbitol and malic acid to stimulate normal salivation and provide temporary relief of dry mouth in patients who have some residual secretory function and taste perception. Numoisyn® Lozenges support saliva s natural protection of teeth so that teeth are not damaged with repeated and use of the lozenges. They are sugar free and buffered with calcium to protect teeth. Numoisyn® Lozenges have been demonstrated to be safe and effective for long-term use and are well tolerated by patients. Use of Numoisyn® Lozenges improves subjective symptoms of dry mouth and does not cause bacteria or plaque formation or loss of tooth enamel hardness.

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Research and Development Pipeline

The table below summarizes our current clinical and preclinical programs.

Program	Indication	Development Status	Target	Cell Cycle Mechanism
Oncology				
Sapacitabine, CYC682	Elderly AML	Phase 2 randomized trial on-going	DNA polymerase	G2 and S phase
Sapacitabine, CYC682	MDS	Phase 2 randomized trial on-going	DNA polymerase	G2 and S phase
Sapacitabine, CYC682	CTCL	Phase 2 randomized trial on-going	DNA polymerase	G2 and S phase
Sapacitabine, CYC682	NSCLC	Phase 2 trial on-going	DNA polymerase	G2 and S phase
Sapacitabine, CYC682	Advanced leukemias and MDS	Phase 1 trial closed to accrual	DNA polymerase	G2 and S phase
Seliciclib, CYC202	NSCLC	Phase 2b randomized trial closed to accrual	CDK2/A, 2/E, 7, 9	G1/S checkpoint and others
Seliciclib, CYC202	NPC	Phase 2 randomized trial. Lead-in phase only on-going	CDK2/A, 2/E, 7, 9	G1/S checkpoint and others
CYC116	Cancer	Phase 1 trial on-going	Aurora kinase & VEGFR2	Mitosis
CDK Inhibitors, Second Generation	Cancer	Preclinical	CDK	G1/S checkpoint and others
Plk1 Inhibitors	Cancer	Preclinical	Plk	G2/M checkpoint
Hdm2 Inhibitors	Cancer	On hold, Not a company priority	Hdm2	G1/2 phase
Cyclin Binding Groove Inhibitors	Cancer	On hold. Not a company priority	Cyclin binding groove	S phase
Other therapeutic areas				
Cell Cycle Inhibitors	Inflammatory Kidney Diseases	Phase 1 trial completed On hold. Not a company priority	CDK	G1/S checkpoint and others
Cell Cycle Inhibitors	HIV/AIDS	On hold. Not a company priority	CDK	Several
GSK-3 Inhibitors	Type 2 Diabetes	On hold. Not a company priority	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 of cancer diagnosed every year. Five common solid 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.

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Acute myeloid leukemia is one of the most common types of leukemia or cancer in the blood and bone marrow. According to the American Cancer Society approximately 44,000 cases of leukemia are diagnosed annually in the United States of which about 13,400 are classified as AML. Leukemia is a deadly disease with an estimated 9,000 deaths annually in the United States, almost all in adults. The average age of a patient with AML is 67 and about two-thirds of AML patients are above 60 years old. The prognosis of AML in the elderly is poor.

Lung cancer is a cancer starting in the lungs that often takes many years to develop. About 85% to 90% of all lung cancers are of the non-small cell type or NSCLC. According to the American Cancer Society an estimated 215,000 patients are diagnosed annually with non-small cell lung cancer in the United States. An estimated 380,000 new cases are diagnosed annually in the European Union. Non-small cell lung cancer is a deadly disease with an estimated 162,000 deaths annually in the United States.

Lymphoma is a cancer of lymphoid tissue, a part of the lymphatic system. Lymphoid tissue is formed by several types of immune system cells that work together mainly to resist infections. About 5% of all lymphomas start in the skin often staying there without spreading to internal organs and are called cutaneous lymphomas. The main cell types found in lymphoid tissue are B lymphocytes and T lymphocytes resulting in B-cell or T-cell lymphoma or CTCL. CTCL causes disfiguring skin lesions and severe itching. According to the American Cancer Society an estimated 3,000 patients are diagnosed annually with lymphoma in the skin in the United States.

NPC develops in the nasopharynx, an area in the back of the nose toward the base of the skull. Although it is sometimes considered a head and neck or an oral cancer, nasopharyngeal cancer is different from these cancers. It is frequently fatal, once the disease recurred after initial chemotherapy and radiotherapy, spreads widely and has different risk factors such as Epstein-Barr virus or EBV infection. High EBV viral titers are considered an indicator of poor prognosis. According to the American Cancer Society an estimated 2,100 patients are diagnosed annually with nasopharyngeal cancer in the United States. An estimated 2,500 are diagnosed annually in the European Union but an estimated 70,000 new cases are diagnosed annually in the Asia Pacific region.

Oncology Development Programs

We are generating several families of anticancer drugs that act on the cell cycle including nucleoside analogues, cyclin dependent kinase or CDK inhibitors and Aurora kinase/Vascular Endothelial Growth Factor Receptor 2 or AK/VEGFR2 inhibitors. Although a number of pharmaceutical and biotechnology companies are currently attempting to develop nucleoside analogues, CDK inhibitor, AK and/or VEGFR inhibitor drugs, we believe that our drug candidates, are differentiated in that they are orally available and interact with unique target profiles and mechanisms. For example we believe that our sapacitabine is the only orally available nucleoside analogue presently being tested in Phase 2 trials in AML, seliciclib is the only orally available CDK inhibitor currently in Phase 2 trial.

In our development programs, we have been an early adopter of biomarker analysis to help evaluate whether our drug candidates are having their intended effect through their assumed mechanisms at different doses and schedules. 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.

Our approach to drug discovery and development has relied on proprietary genomic technology to identify gene targets, which are then progressed by means of structure-based drug design techniques through to the development stage. This approach is exemplified by our Aurora kinase, or AK, and Polo-like kinase, or Plk, inhibitor programs. Fundamentally, this approach to drug discovery and design aims to improve our 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. However, as a result of the reduction in our workforce in September, 2008 our ability to identify, optimize and develop new targets is significantly curtailed.

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Sapacitabine

Our lead 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 with DNA synthesis by causing single-strand DNA breaks and induces arrest of the cell division cycle at G2/M checkpoint. A number of nucleoside drugs, such as gemcitabine, or Gemzar®, from Eli Lilly, cytarabine, also known as Ara-C, a generic drug, 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. We have retained worldwide rights to commercialize sapacitabine with the exception of Japan where Daiichi-Sankyo has a right of first refusal to market the drug under terms to be negotiated.

We are currently exploring sapacitabine in both hematalogic cancers and solid tumors.

Hematologic cancers

Phase 1 clinical trial in patients with advanced leukemias and myelodysplastic syndromes

In December 2007, at the 49th Annual Meeting of the American Society of Hematology or ASH, we reported updated interim results from a Phase 1 clinical trial of oral sapacitabine in patients with advanced leukemias and MDS. Data from this study demonstrated that sapacitabine had a favorable safety profile and promising anti-leukemic activity in patients with relapsed and refractory AML and MDS when administered by two different dosing schedules. The primary objective of the study is to determine the maximum tolerated dose, or MTD of sapacitabine administered twice daily for seven consecutive days every 21 days or three consecutive days per week for two weeks every 21 days. The MTD was reached at 375 mg on the seven-day schedule and 475 mg on the three-day schedule. Dose-limiting toxicity was gastrointestinal which included abdominal pain, diarrhea, small bowel obstruction and neutropenic colitis. One patient treated at the MTD of 375 mg on the seven-day schedule died of complications from neutropenic colitis. Among 46 patients, 42 with AML and 4 with MDS, in this dose escalating study, the best responses were complete remission or CR or complete remission without platelet recovery or CRp in six patients for an Overall Response Rate of 13%. In addition, 15 patients had a significant decrease in bone marrow blasts including seven with blast reduction to 5% or less. The study was run at The University of Texas M. D. Anderson Cancer Center and is led by Dr. Hagop Kantarjian, Professor of Medicine and Chairman of the Leukemia Department and Dr. William Plunkett, Professor and Chief, Section of Molecular and Cellular Oncology, Department of Experimental Therapeutics.

Randomized Phase 2 clinical trial in elderly patients with AML who are previously untreated or in first relapse.

In December 2007, we initiated an open-label, multicenter, randomized Phase 2 clinical trial of oral sapacitabine in elderly patients with AML who are previously untreated or in first relapse. This study follows the encouraging anti-leukemic activity observed in the Phase 1 trial of oral sapacitabine described above. The Phase 2 study is led by Dr. Hagop Kantarjian. The primary objective of this study is to evaluate the 1-year survival rate of three dosing schedules of sapacitabine in elderly patients with previously untreated or first relapsed AML. Secondary objectives are to assess the number of patients who have achieved a CR or CR without blood count recovery, or CRp, duration of CR or CRp, or hematological improvement and their corresponding durations, transfusion requirements, number of hospitalized days and safety.

The study uses a selection design with the objective of identifying a dosing schedule among three different schedules which produces a better one-year survival rate in the event that all three dosing schedules are active. The three dosing schedules are: 200 mg twice daily for seven days every 21 days, 300 mg twice daily for seven days every 21 days and 400 mg twice daily for three days per week for two weeks every 21 days The trial will enroll a total of approximately 60 patients or approximately 20 patients in each arm. The study uses a Bayesian continuous

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monitoring rule to stop accrual in one or more arms of the study in the event that a dosing schedule does not appear to have a sufficient number of responses.

In October 2008, we completed enrollment, as per the protocol in the AML stratum. Interim results from this trial are expected to be available in the first half of 2009 and final results during the second half of 2009.

Randomized Phase 2 clinical trial as a second-line treatment for MDS

In September 2008, we advanced sapacitabine into Phase 2 development as a second-line treatment for MDS. The MDS study is designed as a protocol amendment expanding the ongoing Phase 2 trial of sapacitabine described above, to include a cohort of patients with MDS. MDS are a group of hematologic cancers in which the bone marrow becomes unable to produce a sufficient number of healthy blood cells. Patients with MDS often progress to AML. As with the original Phase 2 study in elderly patients with AML, the primary objective of the MDS stratum is to evaluate the one-year survival rate of three dosing schedules of sapacitabine. Secondary objectives are to assess the number of patients who have achieved a complete remission or CR, complete remission without blood count recovery or CRp, hematological improvement and their corresponding durations, transfusion requirements, number of hospitalization days and safety. The study uses a selection design with the objective of identifying a dosing schedule which produces a better one year survival rate for each stratum in the event that all three dosing schedules are active.

Pivotal trial plan for sapacitabine for the treatment of hematological malignancies.

On February 6, 2009, we announced progress with a pivotal trial plan for sapacitabine for the treatment of hematological malignancies. The announcement followed our recent meeting with the FDA. The pivotal trial plan consists of treating in an open-label, single arm study of approximately 100 patients with AML or MDS on a dosing regimen to be selected from the current ongoing randomized Phase 2 study of oral sapacitabine in elderly patients. We anticipate that the trial will start enrolling patients in such a pivotal study within 2009. Efficacy and safety in a total of approximately 200 patients with leukemia or MDS will be required to provide information for the label in a potential future submission of a New Drug Application or NDA.

Solid tumors

Phase 1 studies

Two Phase 1 studies of sapacitabine were completed in the United States by Daiichi-Sankyo Co., Ltd of Japan, from which we in-licensed sapacitabine, evaluating 87 patients in refractory solid tumors. A Phase 1b dose escalation clinical trial was completed in the United States for the treatment of patients with refractory solid tumors or lymphomas. Preliminary results 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 stromal tumor, and parotid acinar carcinoma.

Phase 2 clinical trial in patients with advanced CTCL

In April 2007, we initiated a Phase 2 clinical trial in patients with advanced CTCL, a cancer of T-lymphocytes, or white blood cells, which causes disfiguring skin lesions and severe itching. The primary objective of the study is to evaluate tolerability and response rate of 50 mg and 100 mg regimens of sapacitabine both twice a day for three days per week for two weeks in a three week cycle in approximately 32 patients with progressive, recurrent, or persistent CTCL on or following two systemic therapies. The study uses a selection design to choose an optimal dose if both are active. Secondary objectives are to assess response duration, time to response, time to progression and relief of pruritus or itching.

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This study has enrolled 15 patients to date at 3 hospital centers. According to recently available and preliminarily analyzed data, the best response by investigator s assessment is partial response in 3 patients.. The study is being expanded to include additional centers.

Phase 2 clinical trial in patients with advanced non-small cell lung cancer or NSCLC

In January, 2009 we announced that we had begun treating patients in a Phase 2, open label, single arm, multicenter clinical trial in patients with NSCLC who have had one prior chemotherapy. This study builds on the observation of prolonged stable disease of four months or longer experienced by heavily pretreated NSCLC patients involved in two Phase 1 studies of sapacitabine. The multicenter Phase 2 trial is led by Philip D. Bonomi, M.D., the Alice Pirie Wirtz Professor of Medical Oncology at the Rush University Medical Center, Chicago.

The primary objective of the study is to evaluate the rate of response and stable disease in patients with previously treated NSCLC. Secondary objectives are to assess progression-free survival, duration of response, duration of stable disease, one year survival, overall survival and safety. The study will enroll approximately 60 patients and has a lead-in phase for dose escalation with the objective of defining a recommended dose followed by a second stage in which patients will be treated at the recommended dose. Study completion is planned to occur approximately six months after the last patient is enrolled.

During May 2008, we received designation from the European Medicines Evaluation Agency or EMEA for sapacitabine as an orphan medicine in two separate indications: AML and MDS. Specifically the EMEA s Committee for Orphan Medicinal Products or COMP adopted a positive opinion on the Company s application to designate sapacitabine as an orphan medicinal product for the indications of AML and MDS. The objective of European orphan medicines legislation is to stimulate research and development of medicinal products for rare diseases by providing incentives to industry. An orphan designation in the European Union confers a range of benefits to sponsor companies including market exclusivity for a period of 10 years, EMEA scientific advice on protocol development, direct access to the centralized procedure for review of marketing authorizations, EMEA fee reductions and eligibility for grant support from European agencies.

Seliciclib

Our second drug candidate, seliciclib, is a novel, first-in-class, orally available, CDK inhibitor. The compound selectively inhibits multiple kinase enzyme targets, specifically 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 300 patients in several Phase 1 and 2 uncontrolled studies and has shown early signs of anti-cancer activity. We have retained worldwide rights to commercialize seliciclib.

Phase 1 studies

We have completed two Phase 1 trials that enrolled 24 healthy volunteers and three Phase 1 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 1 study sponsored and conducted by independent investigators to have clinical antitumor activity in patients with nasopharyngeal cancer or NPC, measured as a decrease in the size of primary tumor

and involved lymph nodes, as well as an increase in tumor cell death by biomarker analyses.

Phase 2 studies

Four Phase 2 trials have been conducted in cancer patients to evaluate the tolerability and antitumor activity of seliciclib alone or in combination with standard chemotherapies used in the treatment of advanced NSCLC, or breast cancer. Interim data from two Phase 2 open-label studies of a total of 52 patients with NSCLC, suggest that

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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.

Phase 2b APPRAISE study as a treatment for patients with advanced NSCLC

Seliciclib is currently being investigated in the Phase 2b APPRAISE study as a treatment for patients with advanced NSCLC. APPRAISE is a double-blinded, randomized study of single agent seliciclib versus best supportive care in patients with NSCLC treated with at least two prior systemic therapies. APPRAISE is led by Chandra P. Belani, M.D. at Milton S. Hershey Medical Center, Penn State University and Alan B. Sandler, M.D. at Vanderbilt-Ingram Cancer Center. The study s main objective is to learn the anti-tumor activity of seliciclib as a single agent in refractory NSCLC and help determine further development strategies. The study design is randomized discontinuation. All patients receive seliciclib at a dose of 1200 mg twice a day for three days for at least three cycles of two weeks each. Patients who achieve stable disease after three cycles will be randomized to continue on seliciclib or receive placebo with best supportive care. Patients in the placebo arm who progress will be given the option to cross-over and again receive seliciclib. The primary efficacy endpoint of APPRAISE is progression free survival, or PFS which will be measured in the randomized portion of the study. To detect a 100% increase in PFS from two to four months 80 randomized patients are required. An interim assessment of safety and efficacy will be performed after approximately 40 patients have been randomized.

On August 28, 2008, we announced that an independent data review committee or IDRC completed a review of the first interim analysis data from the study. The IDRC assessed the safety profile of seliciclib and recommended that the study continue after reviewing data from the 173 patients with previously-treated NSCLC, of whom 45 proceeded into the blinded portion of the study and were randomized to receive either seliciclib or best supportive care.

Based on the interim data, the IDRC reached the following principal conclusions:

There were no safety concerns that would warrant stopping the study;

The study would probably not demonstrate an improvement in progression-free survival as there was no trend favoring the seliciclib treatment arm;

As a definitive conclusion could not be reached because of the low number of events, it was recommended that the study be continued.

We analyzed the committee s conclusions and weighed the costs with the expected benefits of continuing the study and we concluded that we would not enroll additional patients. The trial will continue with the patients already enrolled until the last enrolled patient has completed follow-up. In accordance with the protocol, we remain blinded to the study data until this event has occurred.

Phase 2 multicenter, international, blinded randomized study as a single agent in patients with NPC

In November 2007, we commenced a Phase 2 multicenter, international, blinded randomized study of oral seliciclib as a single agent in patients with NPC. The primary objective is to evaluate 6-month progression free survival, or PFS, of two dosing schedules of seliciclib in approximately 75 patients with previously treated NPC. Secondary objectives are overall survival, response rate, response duration, safety and tolerability. The first part of the study is designed to confirm safety and tolerability of 400 mg twice a day for four days per week or 800 mg once a day for four days per week of seliciclib. It is open to approximately 12 to 24 patients with advanced solid tumors as well as patients with

NPC. The second part of the study is designed to detect major differences between the two dosing schedules of seliciclib and a placebo group in terms of 6-month PFS in approximately 51 patients. The start of the second part of the study is dependant on clinical data from the lead-in phase and resources available to us. The study uses a selection design to choose a better dosing schedule if both seliciclib dosing schedules are active.

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CYC116

In June 2007, we initiated a multicenter Phase 1 pharmacologic clinical trial of CYC116, an orally-available inhibitor of Aurora kinase A and B and VEGFR2, in patients with advanced solid tumors. The multicenter Phase 1 trial, currently on-going, is designed to examine the safety and tolerability of CYC116 in patients with advanced solid tumors. The primary objective of the study is to determine the maximum tolerated dose. Secondary objectives are to evaluate the pharmacokinetic and pharmacodynamic effects of the drug and to document anti-tumor activity. Aurora kinases, or AK, are a family of serine/threonine protein 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. The Aurora kinases were discovered by Professor David Glover, our Chief Scientist. VEGFR2 is a receptor protein that plays a key regulatory role in the angiogenesis pathway, or blood vessel formation. VEGFR is targeted by recently approved drugs such as bevacizumab and sorafenib indicated for the treatment of several solid cancers, such as breast, colorectal, kidney, liver and lung. We have retained worldwide rights to commercialize CYC116.

Other programs

We have allocated limited resources to programs which allow us to maintain and build on our core competency in cell cycle biology and research. In our second generation CDK inhibitor program, we have discovered over 600 novel CDK inhibitors that are members of a different chemical family than seliciclib and we believe may prove to be more potent anticancer agents than seliciclib based on preclinical observations. Our 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. Plk was discovered by Professor David Glover, our Chief Scientist.

The Company has a number of earlier stage programs for which no resources will be allocated in accordance with our revised operating plan announced in September 2008. Where appropriate we intend to progress unfunded programs through collaboration with groups that specialize in the particular mechanism of action or disease areas. These programs are described below.

Hdm2 Inhibitors

One of the key cell cycle regulatory proteins is p53, a protein discovered by our founder, Professor Sir David Lane. 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 cyclin A from binding to its substrates results in cell cycle arrest and induces apoptosis in cancer cells. This was the subject of a two-year collaboration with AstraZeneca that concluded in mid-2003. We have retained all intellectual property rights associated with this program.

Clotrimazole Analogs

We have licensed from Lorus Therapeutics, Inc., or Lorus, 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. On January 9, 2009 we gave notice to terminate the license agreement with Lorus. The termination will be effective four months from the date of notice on May 9, 2009.

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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. The agreement was terminated in 2007; Genzyme has no residual rights in relation to Cyclacel s compounds.

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 in infected host cells and may 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 viral targets and are less likely to induce viral resistance, a major cause of failure of currently available antiviral drugs. We have investigated a number of compounds in this program, some of which appear to reduce HIV levels in biological tests and induce antiviral effects that may be equivalent to many existing HIV/AIDS therapeutic agents. We intend to progress this program through collaboration with groups that specialize in virology research.

GSK-3 Inhibitors in Type 2 Diabetes

Inhibition of Glycogen Synthase Kinase-3 or GSK-3 is an essential element in the body s regulation of blood sugar. GSK-3 regulates the glycogen synthase enzyme that indirectly controls glucose levels. In healthy humans 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 patients with adult onset or Type 2 Diabetes GSK-3 inhibition does not occur resulting in failure of glucose control and the energy storage mechanism. We believe that GSK-3 inhibitor drugs may be suitable for development as Type 2 Diabetes therapies. GSK-3 is a target that is structurally very similar to CDK. We have identified four chemical families of GSK-3 inhibitors some of which are potent at picomolar concentrations which we believe are among the most potent GSK-3 inhibitors disclosed in relevant research literature. We have selected two lead compounds from the series, both of which have achieved proof-of-concept in the standard Zucker rat 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 that specialize in diabetes research.

Business Strategy

During September 2008, we revised our operating plan with the objective of reducing operating expenditure through the streamlining of our pipeline development and reduction in staff numbers. This action allows us to concentrate resources on the development of sapacitabine and possibly realize its commercial potential. As a consequence, all other programs may not realize their commercial potential until funds become available. Although the plan reduced our workforce by approximately 30%, the majority of which were scientists, we are and intend to remain strongly focused on the development of sapacitabine.

Focus on the cell cycle and cancer

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 and

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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 for the following reasons:

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 our sapacitabine is the only orally available nucleoside analogue presently being tested in Phase 2 trials in AML, seliciclib is the only orally available CDK inhibitor currently in Phase 2 trials and CYC116 is the only AK inhibitor in clinical trials that also interacts with VEGFR2. We believe that we are 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 currently retain virtually all marketing rights to the compounds associated with our current clinical-stage drug programs. To optimize our commercial return, we intend to both enter into selected partnering arrangements, and to leverage our sales and marketing capability by retaining co-promotion rights as appropriate. Historically, we have planned to develop compounds through the Phase 2 proof-of-efficacy stage before seeking a partner. We may be prepared to enter into partnering arrangements earlier than Phase 2 proof-of-concept trials in connection with drug programs outside our core competency in oncology.

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 key employees and consultants;

Confidentiality agreements with our employees, consultants, and others having access to its proprietary information;

Standard policies for the maintenance of laboratory notebooks to establish priority of our inventions;

Freedom to use studies from patent counsel;

Material transfer agreements; and

Trademark protection

In addition to our 33 U.S. patents, we own 20 patents that were granted by the European Patent Office, or EPO, for designated European countries, and 37 issued patents in other countries. The European granted patents expire between 2015 and 2026. In addition to the licenses we hold under the 10 patents issued in the United States, we hold licenses under 44 issued patents worldwide, eight granted by the EPO for designated European countries and 36 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 we consider important to our

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business. We usually file first in the United Kingdom and then extend our applications to other countries through the Patent Cooperation Treaty or PCT. In some cases, we file directly in the United States.

We give priority to obtaining substance of matter claims in the United States, the EPO, Japan and other important markets if such protection is available. We prefer substance of matter claims because they give us rights to the compounds themselves, and not merely a particular use. 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 31 patent applications pending in the United States, 32 before the EPO, five pending PCT applications still in the international application phase, and over 170 pending patent applications in other countries. Six 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 certain patents that directly relate to business strategy. In addition to the pending patent applications referred to above that we own, there are 11 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 PCT filings covering derivative compounds, medical uses and related technology. The first patent application from this family have resulted in the issuance of two U.S. patents with substance of matter claims covering a specific genus of compounds showing activity in preclinical and discover 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 our Fluorescience fluorescent assay techniques Penetratin, a drug delivery system. In addition, 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 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 our 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 understand that others may exist, that could support claims that, if granted, would cover various aspects of our developmental programs, including in

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some cases particular uses of our lead drug candidates, sapacitabine, seliciclib, CYC116, 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 uses of sapacitabine and seliciclib that are not part of our 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 related 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. 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 us 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.

Sapacitabine

We have entered into a license agreement with Daiichi-Sankyo Co., Ltd. of Japan or Daiichi-Sankyo with respect to patents and patent applications covering the sapacitabine compound. We have filed patent applications claiming polymorphic forms of sapacitabine and methods for its preparation and use as well as related know-how and materials. The Daiichi-Sankyo agreement commenced on September 10, 2003. The issued patents for the sapacitabine compound cover the United States, EPO, Japan and 20 other countries. These patents expire between 2012 and 2014. The issued patents for the polymorphic forms cover the United States, EPO, Japan and six other countries, with patents pending in a further seven countries. These patents expire in 2022. 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 Daiichi-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 Daiichi-Sankyo an up-front fee, reimbursement for Daiichi-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 reimbursements have been paid. Royalties are payable in each country for the term of patent protection in the country or for ten years following the first commercial sale of licensed products in the country, whichever is later. Royalties are payable on 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 owed under it. If we wish to appoint a third party to develop or commercialize a sapacitabine-based product in Japan, within certain limitations,

Daiichi-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 or twelve if after launch of sapacitabine-based product or by either party for material default. On termination, if Daiichi-Sankyo wishes to acquire an exclusive license to sapacitabine

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intellectual property developed by us during the term of the license, Daiichi-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.

Seliciclib

We have entered into an agreement with Centre National de Recherche Scientifique, or CNRS, and Institut Curie that grants us 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. We paid an up-front fee and yearly payments and milestone payments until the patents covering the seliciclib compound, particular uses of the compound, and particular uses and derivatives of the compound were published as granted in either the United States or by EPO which occurred in 2001 and 2003, respectively. Milestones are also payable on the first commercialization of a product that consists of a new chemical entity that is covered by one of the licensed patents.

We will be obligated to pay royalties based on our net sales of products covered by the patents. 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 of Experimental Botany and CNRS. The patents have been issued in the United States and by the EPO 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 of Experimental Botany, CNRS has the exclusive right to enter into license agreements covering the patents. The agreement reserves to both CNRS

and the Czech Institute of Experimental Botany certain rights, including the right to patent improvements and to use the patents for internal research purposes.

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Clotrimazole Analogs and CYC381

We entered into a license agreement with NuChem Pharmaceuticals, Inc., or NuChem 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 EPO, Japan and other countries, as well as related know-how, materials and technology. The effective date of the agreement is September 22, 2003. On January 9, 2009 we gave notice to terminate the license agreement with Lorus. The termination will be effective four months from the date of notice on May 9, 2009.

Sinclair Pharma plc

Through the acquisition of ALIGN we acquired from Sinclair Pharma plc, or Sinclair, U.S. and Canadian licensing rights to the three commercial drugs marketed by ALIGN Xclair® Cream, Numoisyn® Liquid and Numoisyn® Lozenges. All three products were launched in the United States in January 2006. Each of the agreements covering the three license rights expire in June 2015. Under these agreements, we have obligations to pay certain quarterly royalties and other amounts pursuant to the agreement which may be reduced or lapse if we exceed certain sales levels.

Manufacturing

We have no in-house manufacturing capabilities and have no current plans to establish manufacturing facilities for significant clinical or commercial production. We have no direct experience in manufacturing commercial quantities of any of our products, and we currently lack the resources or capability to manufacture any of our products on a clinical or commercial scale. As a result, we are dependent on corporate partners, licensees or other third parties for the manufacturing of clinical and commercial scale quantities of all of our products. We believe that this strategy will enable us to direct operational and financial resources to the development of our product candidates rather than diverting resources to establishing a manufacturing infrastructure.

Sinclair contracts with third party manufacturers to supply finished goods that meet our needs with respect to Xclair® Cream, Numoisyn® Liquid and Numoisyn® Lozenges. If any of Sinclair s third party manufacturers service providers do not meet our or our licensor s requirements for quality, quantity or timeliness, or do not achieve and maintain compliance with all applicable regulations, demand for our products or our ability to continue supplying such products could substantially decline.

Sales and Marketing

We currently have a nine person pharmaceutical commercial sales organization marketing our ALIGN products. We expect to expand our sales and commercialization group to support our products that may be commercialized for oncology/hematology indications and possibly other therapeutic areas. We intend to market and sell directly products for indications addressing modest patient populations. For products with indications addressing large patient populations we may partner with other pharmaceutical companies. In addition, we may accelerate the expansion of our commercial organization to take advantage of any product in-licensing and acquisition opportunities that we may we elect to pursue.

Government Regulation

The 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 commercialized 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:

- 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;

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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 NDA, to the FDA;

satisfactory completion of an FDA pre-approval inspection of the manufacturing facilities at which the product is produced to assess compliance with current good manufacturing practice GMP, or cGMP, regulations;

FDA review and approval of the NDA prior to any commercial marketing, sale or shipment of the drug; and

Regulation of commercial marketing and sale of drugs.

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 1: 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 1 clinical trial typically designed to evaluate the impact of the drug candidate in combination with currently approved drugs.

Phase 2: 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 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more expensive Phase 3 clinical trial.

Phase 3: These clinical trials are commonly referred to as pivotal clinical trials. If the Phase 2 clinical trials demonstrate that a dose range of the drug candidate is effective and has an acceptable safety profile, Phase 3 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.

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

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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 3 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 4 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 suggest or in any way guarantee that 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 4 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. In rare instances FDA may grant accelerated approval of an NDA based on Phase 2 data and require confirmatory Phase 3 studies to be conducted after approval and/or as a condition of maintaining approval. We can give no assurance that any of our drugs will be reviewed under such procedures.

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When appropriate, we and our collaborators may attempt 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.

510(k). Section 510(k) of the Food, Drug and Cosmetic Act requires device manufacturers to notify FDA, at least ninety days in advance, of their intent to market a medical device. This is known as Premarket Notification, or PMN, or 510(k). It allows the FDA to determine whether the device is equivalent to a device already placed into one of three classification categories. Medical device manufacturers are required to submit a premarket notification if they intend to introduce a device into commercial distribution for the first time or reintroduce a device that will be significantly changed or modified to the extent that its safety or effectiveness could be affected. Such change or modification could relate to the design, material, chemical composition, energy source, manufacturing process, or intended use.

Other regulatory requirements. Any products 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 cGMP, 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 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 product from distribution, or withdraw approval of that product.

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.

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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.

For our ALIGN products we believe that Beiersdorf, Daiichi-Sankyo, Eisai, Johnson & Johnson, MPM Medical and other companies market products for radiation dermatitis and xerostomia. A large number of drug candidates are in development for the treatment of leukemia, lymphomas, lung cancer and nasopharyngeal cancer. Several pharmaceutical and biotechnology companies have nucleoside analogs on the market or in clinical trials for oncology indications, including Eli Lilly, Genzyme, GlaxoSmithKline and Mayne Pharma. We believe that we are currently the only company that has an orally available CDK-specific agent in Phase 2 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, Piramal Life Sciences Ltd, 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 2 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 2 trial and that Sanofi-Aventis has reinitiated development of alvocidib in Phase 3 clinical trials in patients with chronic leukemia. 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, Merck-Serono, Millennium, Nerviano Medical Sciences, Pfizer and Sunesis have commenced Phase 2 or Phase 1 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, GlaxoSmithKline and Onconova have commenced Phase 1 or Phase 2 clinical trials with Plk inhibitor candidates for oncology indications.

Employees

As of February 15, 2009, we had 51 full-time employees, comprised of 28 employees in research and development and 23 employees in selling, general 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. On September 16, 2008, we announced a revision of our operating plan that concentrates our resources on the advancement of our lead drug, sapacitabine, while maintaining our core competency in drug discovery and cell cycle biology. The plan reduced the workforce across all locations by 25 people.

Available information

We have filed reports, proxy statements and other information with the SEC. Copies of Cyclacel s reports, proxy statements and other information may be inspected and copied at the public reference facilities maintained by the SEC at SEC Headquarters, Public Reference Section, 100 F Street, N.E., Washington D.C. 20549 on official business days during the hours of 10:00 am to 3:00 pm . The public may obtain information on the operation of the SEC s Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC maintains a website that contains

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reports, proxy statements and other information regarding Cyclacel. The address of the SEC website is http://www.sec.gov. We will also provide copies of our Forms 8-K, 10-K, 10-Q, proxy statements and Annual Report at no charge through our website at www.cyclacel.com as soon as reasonably practicable after filing electronically such material with the SEC. Copies are also available, without charge, from Cyclacel Pharmaceuticals, Inc., 200 Connell Drive, Suite 1500, Berkeley Heights, NJ 07922.

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 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 company.

Capital markets are currently experiencing a period of disruption and instability, which has had and could continue to have a negative impact on the availability and cost of capital.

The general disruption in the United States capital markets has impacted the broader worldwide financial and credit markets and reduced the availability of debt and equity capital for the market as a whole. These global conditions could persist for a prolonged period of time or worsen in the future. Our ability to access the capital markets may be restricted at a time when we would like, or need, to access those markets, which could have an impact on our flexibility to react to changing economic and business conditions. The resulting lack of available credit, lack of confidence in the financial sector, increased volatility in the financial markets could materially and adversely affect the cost of debt financing and the proceeds of equity financing may be materially adversely impacted by these market conditions.

The current economic conditions and financial market turmoil could adversely affect our business and results of operations.

Economic conditions remain difficult with the continuing deterioration in the global credit markets, the financial services industry and the United States capital markets and with the United States economy as a whole experiencing a period of substantial turmoil and uncertainty characterized by unprecedented intervention by the United States federal government and the failure, bankruptcy, or sale of various financial and other institutions. We believe the current economic conditions and financial market turmoil could adversely affect our operations, business and prospects, as well as our ability to obtain funds and manage our liquidity. If these circumstances persist or continue to worsen, our future operating results could be adversely affected, particularly relative to our current expectations.

We are at an early stage of development as a company and we do not have, and may never have, any products that generate significant 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. While we have earned modest product revenues from the ALIGN business acquired in October 2007, since beginning operations in 1996, we have not generated any product revenues from our product candidates currently in development. We cannot guarantee that any of our product candidates currently in development will ever become marketable products and we do not anticipate material revenues from the ALIGN products in the foreseeable future. We must demonstrate that our drug candidates satisfy rigorous standards of safety and efficacy for their intended uses before the 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. Sapacitabine and seliciclib, our most advanced drug candidates for the treatment of cancer, are currently our only drug candidates in Phase 2 clinical

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trials. CYC116 is currently in a Phase 1 clinical trial. 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 we 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 from our product candidates currently in development, if any, will be derived from sales of drugs that will not 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 1996 due to costs incurred in connection with our research and development activities and selling, general and administrative costs associated with our operations, and we may never achieve profitability. As of December 31, 2008, our accumulated deficit was $202.7 million. Our net loss for the years ended December 31, 2007 and 2008 was $24.1 million and $40.4 million, respectively. Our net loss attributable to common shareholders from inception through December 31, 2008 was $240.8 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, commercialize any approved drugs and market and promote the ALIGN products: Xclair® Cream, Numoisyn® Liquid and Numoisyn® Lozenges. If our 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, particularly in light of the current economic conditions, 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 to fund 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, licensing revenue, government grants, research and development tax credits and product revenue. 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 may cause our stockholders 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, particularly in light of the current economic conditions. 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.

Due to restrictions under United States securities laws, we have limited ability to utilize our existing shelf registration statement to raise additional capital for a period of up to one year unless the market value of our common stock increases substantially, which would delay or prevent us from raising capital under our existing shelf registration statement. There can be no assurance that our efforts to raise additional funds will be successful, or that sufficient funds will be available on satisfactory terms.

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Our committed equity financing facility with Kingsbridge may not be available to us if we elect to make a draw down, may require us to make additional blackout or other payments to Kingsbridge, and may result in dilution to our stockholders.

On December 10, 2007, we entered into the committed equity financing facility, or CEFF, with Kingsbridge Capital Limited, or Kingsbridge. The CEFF entitles us to sell and obligates Kingsbridge to purchase the lesser of 4,084,590 shares of our common stock or $60 million of our common stock, during the next three years, subject to certain conditions and restrictions. Kingsbridge will not be obligated to purchase shares under the CEFF unless certain conditions are met, which include a minimum price for our common stock; the accuracy of representations and warranties made to Kingsbridge; compliance with laws; effectiveness of the registration statement; and the continued listing of our stock on The NASDAQ Global Market. As the price of our common stock has traded for some months below the minimum price required under the CEFF agreement and we have no certainty that the price of our common stock will exceed the minimum price requirements, we may never be able to access the funds available to us under the CEFF.

In addition, Kingsbridge is permitted to terminate the CEFF if it determines that a material and adverse event has occurred affecting our business, operations, properties or financial condition and if such condition continues for a period of 10 days from the date Kingsbridge provides us notice of such material and adverse event.

If we are unable to access funds through the CEFF, or if the CEFF is terminated by Kingsbridge, we may be unable to access capital on favorable terms or at all.

We are entitled, in certain circumstances, to deliver a blackout notice to Kingsbridge to suspend the use of the registration statement which became effective in December 2007, and prohibit Kingsbridge from selling shares. If we deliver a blackout notice in the 15 trading days following the settlement of a draw down, or if the registration statement is not effective in circumstances not permitted by the agreement, then we must make a payment to Kingsbridge, or issue Kingsbridge additional shares in lieu of this payment, calculated on the basis of the number of shares held by Kingsbridge exclusive of shares that Kingsbridge may hold pursuant to exercise of the Kingsbridge warrant and the change in the market price of our common stock during the period in which the use of the registration statement is suspended. If the trading price of our common stock declines during a suspension of the registration statement, the blackout or other payment could be significant.

Should we sell shares to Kingsbridge under the CEFF, or issue shares in lieu of a blackout payment, it will have a dilutive effective on the holdings of our current stockholders, and may result in downward pressure on the price of our common stock. If we draw down under the CEFF, we will issue shares to Kingsbridge at a discount of up to 10% from the volume weighted average price of our common stock. If we draw down amounts under the CEFF when our share price is decreasing, we will need to issue more shares to raise the same amount than if our stock price was higher. Issuances in the face of a declining share price will have an even greater dilutive effect than if our share price were stable or increasing, and may further decrease our share price.

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;

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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, sales 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.

If we are not able to secure additional funding when needed, especially in light of the current economic conditions and financial market turmoil, 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.

If we do not realize the expected benefits from the restructuring that we announced in September 2008, our operating results and financial conditions could be negatively impacted.

In September 2008, we announced a strategic restructuring designed to focus our resources on our lead drug, sapacitabine, while maintaining the Company s core competency in drug discovery and cell cycle biology. We cannot guarantee that we will not have to undertake additional restructuring activities, that any of our restructuring efforts will be successful, or that we will be able to realize the cost savings and other anticipated benefits from our restructuring. If we are unable to realize the expected operational efficiencies from our restructuring, our operating results and financial condition could be adversely affected.

Any future workforce and expense reductions may have an adverse impact on our internal programs, strategic plans, our ability to hire and retain key personnel and may be distracting to our management.

Further workforce and expense reductions additional to that carried out in September 2008 could result in significant delays in implementing our strategic plans. In addition, employees, whether or not directly affected by such reduction, may seek future employment with our business partners or competitors. Although our employees are required to sign a confidentiality agreement at the time of hire, the confidential nature of certain proprietary information may not be maintained in the course of any such future employment. Further, we believe that our future success will depend in large part upon our ability to attract and retain highly skilled personnel. We may have difficulty retaining and

attracting such personnel as a result of a perceived risk of future workforce and expense reductions. In addition, the implementation of expense reduction programs may result in the diversion of the time and attention of our executive management team and other key employees, which could adversely affect our business.

Budget constraints resulting from our restructuring plan may negatively impact our research and development, forcing us to delay our efforts to develop certain product candidates in favor of developing others, which may prevent us from commercializing our product candidates as quickly as possible.

Research and development is an expensive process. As part of our restructuring plan, we have decided to focus our clinical development priorities on sapacitabine, while still possibly continuing to progress additional programs pending the availability of clinical data and the availability of funds, at which time we will determine the feasibility

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of pursuing the advanced development of seliciclib and CYC116. Because we have had to prioritize our development candidates as a result of budget constraints, we may not be able to fully realize the value of our product candidates in a timely manner, if at all.

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.

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

Some of our costs and expenses are denominated in foreign currencies. Most of our foreign expenses are associated with our research and development operations of our United Kingdom-based wholly-owned subsidiary. When the U.S. dollar weakens against the British pound, the United States dollar value of the foreign-currency denominated expense increases, and when the United States dollar strengthens against the British pound, the United States dollar value of the foreign-currency denominated expense decreases. Consequently, changes in exchange rates, and in particular a weakening of the United States dollar, may adversely affect our results of operations.

We are exposed to risk related to the marketable securities we purchase.

We invest cash not required to meet short term obligations in short term marketable securities. We purchase securities in the United States government, government-sponsored agencies and highly rated corporate and asset-backed securities subject to an approved investment policy. Historically, investment in these securities has been highly liquid and has experienced only very limited defaults. However, recent volatility in the financial markets has created additional uncertainty regarding the liquidity and safety of these investments. Although we believe our marketable securities investments are safe and highly liquid, we cannot guarantee that our investment portfolio will not be negatively impacted by recent or future market volatility.

Clinical trials are expensive, time consuming, subject to delay and may be required to continue beyond our available funding.

Clinical trials are expensive and complex and can take many years and have uncertain outcomes. We estimate that clinical trials of our most advanced drug candidates may be required to continue beyond our available funding and may take several years more 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 because of competition for patients from other trials or other reasons;

negative or inconclusive results from clinical trials;

unforeseen safety issues;

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uncertain dosing issues;

approval and 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;

inability or unwillingness of medical investigators to follow our clinical protocols; and

unavailability of clinical trial supplies.

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.

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 serious adverse events 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 drug candidate seliciclib and neutropenia and gastric-intestinal toxicity was observed in patients receiving sapacitabine. In addition, we may pursue clinical trials for sapacitabine and 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. 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 AKs 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 CDK and AK. One of our drug candidates, seliciclib, is a CDK inhibitor, and CYC116 is an AK and VEGFR2 inhibitor, based on our understanding of CDK and AK inhibitors.

Although a number of pharmaceutical and biotechnology companies are attempting to develop CDK or AK inhibitor drugs for the treatment of cancer, no CDK or AK 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 AK inhibitors in regulating the cell cycle is incorrect seliciclib and CYC116 may fail to produce therapeutically relevant results hindering our ability to pursue our clinical and regulatory strategy.

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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.

Due to our reliance on contract research organizations or other third parties to conduct clinical trials, we may be 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, contract clinical research associates, 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 2 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;

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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 or devices we may develop or sell.

We do not currently operate manufacturing facilities for clinical or commercial production of our drug candidates under development or our currently marketed ALIGN products. We currently lack the resources or the capacity to manufacture any of our products on a clinical or commercial scale. We depend upon a third party, Sinclair, to manufacture the commercial products sold by our ALIGN subsidiary and we can not rely upon Sinclair to continue to supply the products. We anticipate future reliance on a limited number of third party manufacturers until we are able, or decide, to expand our operations to include manufacturing capacities. Any performance failure on the part of manufacturers could delay late stage clinical development or regulatory approval of our drug, the commercialization of our drugs or our ability to sell our commercial products, producing additional losses and depriving us of potential product revenues.

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. 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.

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

In order to execute our business strategy, 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 and key relationships could impair our drug development and commercialization efforts.

We are highly dependent on our senior management and key scientific, technical and sales and marketing personnel. Competition for these types of personnel is intense. The loss of the services of any member of our senior management,

scientific, technical or sales or marketing 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 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. With the acquisition of ALIGN, the success of the commercialization of those products depends, in large part, on our continued ability to develop and maintain important relationships with

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leading key distributors and research and medical institutions. Failure to do that could have a material adverse effect on our ability to commercialize the ALIGN products.

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 and medical devices. 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.

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 an 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, or IND, which must become effective before human clinical trials may begin. Clinical development typically involves three phases of study: Phase 1, 2 and 3. The most significant costs associated with clinical development are the Phase 3 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.

If regulatory agencies do not accept our proposed registration pathways based on Phase 2 data, then we will likely need to conduct large pivotal studies, which are time-consuming and expensive.

Regulatory agencies including but not limited to the FDA, have in certain instances accepted Phase 2 data from uncontrolled studies, as sufficient for approval in indications where an unmet medical need exists or in exceptional

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circumstances. If regulatory agencies, including but not limited to FDA, determine that the design or results of our Phase 2 studies are not sufficient for approval of our investigational drugs, we will likely need to undertake large, controlled pivotal studies, including randomized studies, which are time-consuming and expensive. Because we have limited resources, and research and development is an expensive process, any such requirements may adversely impact our operating results and financial condition and delay our ability to commercialize our drug candidates.

If the results of our studies do not meet the minimal level of statistical significance or other requirements of the FDA, or other regulatory agencies, we will likely need to undertake placebo-controlled Phase 3 studies, which are time-consuming and expensive. Because we have limited resources, and research and development is an expensive process, any such requirements by the FDA may adversely impact our operating results and financial condition and delay our ability to commercialize our lead drug candidate.

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 adversely affect our business.

With regard to the ALIGN products, and following regulatory approval of any of our drug candidates, we are subject to ongoing regulatory obligations and restrictions, which may result in significant expense and limit our ability to commercialize our potential products.

With regard to our ALIGN products and our drug candidates, if any, approved by the FDA or by another regulatory authority, we are 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 product or drug candidate, including adverse events of unanticipated severity or frequency, may result in restrictions on the marketing of the drug or device, and could include withdrawal of the drug or device 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 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, we 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 the rights to 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 Daiichi-Sankyo. 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.

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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 several companies are developing drugs targeting cancer that may compete with our candidates. A large number of drug candidates are in development for the treatment of leukemias, lymphomas, lung cancer and nasopharyngeal cancer. Several pharmaceutical and biotechnology companies have nucleoside analogs on the market or in clinical trials for oncology indications, including Eli Lilly, Genzyme, GlaxoSmithKline and Mayne Pharma. We believe that we are currently the only company that has an orally available CDK inhibitor in Phase 2 clinical trials. 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 2 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 2 trial and that Sanofi-Aventis has reinitiated development of alvocidib in Phase 3 clinical trials in patients with chronic leukemia. 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, Merck-Serono, Millennium and Sunesis have commenced Phase 2 or Phase 1 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, GlaxoSmithKline and Onconova have commenced Phase 1 or Phase 2 clinical trials with Plk inhibitor candidates for oncology indications. We believe that Beiersdorf, Daiichi-Sankyo, Eisai, Johnson & Johnson, MPM Medical and other companies market products for radiation dermatitis and xerostomia.

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 product 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 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 the ALIGN products and our drug candidates depends upon their market acceptance among physicians, patients, healthcare providers and payors and the medical community.

It is necessary that our and our distribution partners products, including Xclair® Cream, Numoisyn® Liquid and Numoisyn® Lozenges achieve and maintain market acceptance. 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 or devices 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;

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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.

If we are unable to compete successfully in our market place, it will harm our business.

There are existing products in the marketplace that compete with our products. Companies may develop new products that compete with our products. Certain of these competitors and potential competitors have longer operating histories, substantially greater product development capabilities and financial, scientific, marketing and sales resources. Competitors and potential competitors may also develop products that are safer, more effective or have other potential advantages compared to our products. In addition, research, development and commercialization efforts by others could render our products obsolete or non-competitive. Certain of our competitors and potential competitors have broader product offerings and extensive customer bases allowing them to adopt aggressive pricing policies that would enable them to gain market share. Competitive pressures could result in price reductions, reduced margins and loss of market share. We could encounter potential customers that, due to existing relationships with our competitors, are committed to products offered by those competitors. As a result, those potential customers may not consider purchasing our products.

There is uncertainty related to coverage, reimbursement and payment by healthcare providers and payors for the ALIGN products and newly approved drugs, if any. The inability or failure to obtain or maintain coverage could affect our ability to market the ALIGN products and 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 the ALIGN products and our drug candidates in both the United States and international markets is substantially dependent on whether third party coverage and reimbursement is available. The United States 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 its potential drugs. The ALIGN products and our drug candidates may not be considered cost-effective and reimbursement may not be available to consumers or may not be sufficient to allow the ALIGN products or 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 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.

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We may be exposed to product liability claims that may damage our reputation and we 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 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.

Following the acquisition of ALIGN, we now market commercialized products, and consequently we are exposed to additional risks of product liability claims. These risks exist even with respect to drugs and devices 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 have secured limited product liability insurance coverage, but may not be able to maintain such insurance on acceptable terms with adequate coverage, or at a 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 exceed insurance coverage creating 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.

We may be required to defend lawsuits or pay damages in connection with the alleged or actual violation of healthcare statutes such as fraud and abuse laws, and our corporate compliance programs can never guarantee that we are in compliance with all relevant laws and regulations.

Our commercialization efforts in the United States are subject to various federal and state laws pertaining to promotion and healthcare fraud and abuse, including federal and state anti-kickback, fraud and false claims laws.

Anti-kickback laws make it illegal for a manufacturer to offer or pay any remuneration in exchange for, or to induce, the referral of business, including the purchase of a product. The federal government has published many regulations relating to the anti-kickback statutes, including numerous safe harbors or exemptions for certain arrangements. False claims laws prohibit anyone from knowingly and willingly presenting, or causing to be presented for payment to third-party payers including Medicare and Medicaid, claims for reimbursed products or

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services that are false or fraudulent, claims for items or services not provided as claimed, or claims for medically unnecessary items or services.

Our activities relating to the sale and marketing of our products will be subject to scrutiny under these laws and regulations. It may be difficult to determine whether or not our activities, comply with these complex legal requirements. Violations are punishable by significant criminal and/or civil fines and other penalties, as well as the possibility of exclusion of the product from coverage under governmental healthcare programs, including Medicare and Medicaid. If the government were to investigate or make allegations against us or any of our employees, or sanction or convict us or any of our employees, for violations of any of these legal requirements, this could have a material adverse effect on our business, including our stock price. Our activities could be subject to challenge for many reasons, including the broad scope and complexity of these laws and regulations, the difficulties in interpreting and applying these legal requirements, and the high degree of prosecutorial resources and attention being devoted to the biopharmaceutical industry and health care fraud by law enforcement authorities. During the last few years, numerous biopharmaceutical companies have paid multi-million dollar fines and entered into burdensome settlement agreements for alleged violation of these requirements, and other companies are under active investigation. Although we have developed and implemented corporate and field compliance programs as part of our commercialization efforts, we cannot assure you that we or our employees, directors or agents were, are or will be in compliance with all laws and regulations or that we will not come under investigation, allegation or sanction.

In addition, we may be required to prepare and report product pricing-related information to federal and state governmental authorities, such as the Department of Veterans Affairs and under the Medicaid program. The calculations used to generate the pricing-related information are complex and require the exercise of judgment. If we fail to accurately and timely report product pricing-related information or to comply with any of these or any other laws or regulations, various negative consequences could result, including criminal and/or civil prosecution, substantial criminal and/or civil penalties, exclusion of the approved product from coverage under governmental healthcare programs including Medicare and Medicaid, costly litigation and restatement of our financial statements. In addition, our efforts to comply with this wide range of laws and regulations are, and will continue to be, time-consuming and expensive.

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 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

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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.

Intellectual property rights of third parties may increase our costs or delay or prevent us from being able to commercialize our drug candidates and/or the ALIGN products.

There is a risk that we 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 of our research and/or the ALIGN products. 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. 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 sapacitabine and seliciclib that are not part of our current clinical programs for these compounds. Numerous third-party United States and foreign issued patents and pending applications exist in the area of kinases, including CDK, AK and Plk for which we have research programs. 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. 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. 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. 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 to 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 our aurora kinase inhibitors once clinical trials are completed.

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;

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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 CNRS and Institut Curie. Both of these license agreements impose payment and other material obligations on us. Under the Daiichi-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. 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. 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 adversely affect our business.

We incur increased costs and management resources as a result of being a public company, and we still may fail to comply with public company obligations.

As a public company, we face and will continue to face increased legal, accounting, administrative and other costs and expenses as a public company that we would 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 concluded that as of December 31, 2008, our internal control over financial reporting is effective. As our business grows and changes, there can be no assurances that we can maintain the effectiveness of our internal controls over financial reporting.

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 that are both related and unrelated to the operating performance of the individual companies. In addition, the stock market as a whole and biotechnology and other life science stocks in particular have experienced significant recent volatility. Like our common stock, these stocks have experienced significant price and volume fluctuations for reasons unrelated to the operating performance of the individual companies. In addition, due to our

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existing stock price, we may not continue to qualify for continued listing on the NASDAQ Global Market. To maintain listing, we are required, among other things, to maintain a minimum closing bid price of $1.00 per share. On October 16, 2008 NASDAQ temporarily suspended enforcement of its continued listing requirements rules requiring a minimum $1.00 closing bid price and market value of publicly held shares for listing on the NASDAQ Stock Market until January 16, 2009. On December 18, 2008, NASDAQ extended its temporary suspension through April 19, 2009. 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 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.

If securities or industry analysts do not publish research or reports about us, if they change their recommendations regarding our stock adversely or if our operating results do not meet their expectations, our stock price and trading volume could decline.

The trading market for our common stock is influenced by the research and reports that industry or securities analysts publish about us. If one or more of these analysts cease coverage of us or fail to regularly publish reports on us, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline. Moreover, if one or more of the analysts who cover us downgrade our stock or if our operating results do not meet their expectations, our stock price could 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 million 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.

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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.

Certain severance-related agreements in our executive employment agreements may make an acquisition more difficult and could result in the entrenchment of management.

In March 2008 (as amended in December 2008 with respect to our President and Chief Executive Officers), we entered into employment agreements with our President and Chief Executive Officer and our Executive Vice President, Finance, which contain severance arrangements in the event that such executive s employment is terminated without cause or as a result of a change of control (as each such term is defined in each agreement). The financial obligations triggered by 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.

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 amended and restated 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 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 convertible preferred stock may only be paid from surplus or, if there is no surplus, from

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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 or we may choose to suspend the payment of dividends. 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. In addition, due to our existing stock price, we may not continue to qualify for continued listing on the NASDAQ Global Market. To maintain listing, we are required, among other things, to maintain a minimum closing bid price of $1.00 per share. On October 16, 2008 NASDAQ temporarily suspended enforcement of its continued listing requirements rules requiring a minimum $1.00 closing bid price and market value of publicly held shares for listing on the NASDAQ Stock Market until January 16, 2009. On December 18, 2008, NASDAQ extended its temporary suspension through April 19, 2009.

The future sale of our common and convertible preferred stock, and future issuances of our common stock upon conversion of our convertible preferred stock 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.

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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 the holders of the securities 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 automatically convert the convertible preferred stock into common stock if the closing price of our common stock has exceeded $35.30. 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.

The number of shares of common stock which are registered, including the shares to be issued upon exercise of our outstanding warrants, is significant in relation to our currently outstanding common stock and could cause downward pressure on the market price for our common stock.

The number of shares of common stock registered for resale, including those shares which are to be issued upon exercise of our outstanding warrants, is significant in relation to the number of shares of common stock currently outstanding. If the security holder determines to sell a substantial number of shares into the market at any given time, there may not be sufficient demand in the market to purchase the shares without a decline in the market price for our common stock. Moreover, continuous sales into the market of a number of shares in excess of the typical trading volume for our common stock, or even the availability of such a large number of shares, could depress the trading market for our common stock over an extended period of time.

If persons engage in short sales of our common stock, including sales of shares to be issued upon exercise of our outstanding warrants, the price of our common stock may decline.

Selling short is a technique used by a stockholder to take advantage of an anticipated decline in the price of a security. In addition, holders of options and warrants will sometimes sell short knowing they can, in effect, cover through the exercise of an option or warrant, thus locking in a profit. A significant number of short sales or a large volume of other sales within a relatively short period of time can create downward pressure on the market price of a security. Further sales of common stock issued upon exercise of our outstanding warrants could cause even greater declines in the price of our common stock due to the number of additional shares available in the market upon such exercise, which could encourage short sales that could further undermine the value of our common stock. You could, therefore,

experience a decline in the value of your investment as a result of short sales of our common stock.

Our distribution rights to the ALIGN products are licensed from others, and any termination of that license could harm our business.

We have in-licensed from Sinclair the distribution rights to the ALIGN products. This license agreement imposes obligations on us. Although we are currently in compliance with all of our material obligations under this

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license, if we were to breach any such obligations, Sinclair would be permitted to terminate the license. This would restrict us from distributing the ALIGN products.

If our supplier upon whom we rely fails to produce on a timely basis the finished goods in the volumes that we require or fails to meet quality standards and maintain necessary licensure from regulatory authorities, we may be unable to meet demand for our products, potentially resulting in lost revenues.

Our licensor and supplier Sinclair contracts with third party manufacturers to supply the finished goods to us to meet our needs. If any of Sinclair s third party manufacturers service providers do not meet our or our licensor s requirements for quality, quantity or timeliness, or do not achieve and maintain compliance with all applicable regulations, demand for our products or our ability to continue supplying such products could substantially decline. As the third party manufacturers are the sole supplier of the products any delays may impact our sales.

In all the countries where we sell or may sell our products, governmental regulations exist to define standards for manufacturing, packaging, labeling and storing. All of our suppliers of raw materials and contract manufacturers must comply with these regulations. Failure to do so could result in supply interruptions. In the United States, the FDA requires that all suppliers of pharmaceutical bulk material and all manufacturers of pharmaceuticals for sale in or from the United States achieve and maintain compliance with the FDA s Current Good Manufacturing Practice or cGMP regulations and guidelines. Failure of our third-party manufacturers to comply with applicable regulations could result in sanctions being imposed on them or us, including fines, injunctions, civil penalties, disgorgement, suspension or withdrawal of approvals, license revocation, seizures or recalls of products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products. In addition, before any product batch produced by our manufacturers can be shipped, it must conform to release specifications pre-approved by regulators for the content of the pharmaceutical product. If the operations of one or more of our manufacturers were to become unavailable for any reason, any required FDA review and approval of the operations of an alternative supplier could cause a delay in the manufacture of our products.

Our customer base is highly concentrated.

Our principal customers are a small number of wholesale drug distributors. These customers comprise a significant part of the distribution network for pharmaceutical products in the United States. Three large wholesale distributors, AmerisourceBergen Corporation, Cardinal Health, Inc. and McKesson Corporation, control a significant share of the market in the United States. Our ability to distribute any product, including Xclair® Cream, Numoisyn® Liquid and Numoisyn® Lozenges and to recognize revenues on a timely basis is substantially dependent on our ability to maintain commercially reasonable agreements with each of these wholesale distributors and the extent to which these distributors, over whom we have no control, comply with such agreements. Our agreements with wholesaler distributors may contain terms that are not favorable, given our relative lack of market leverage as a company with only three approved products or other factors, which could adversely affect our commercialization of Xclair® Cream, Numoisyn® Liquid and Numoisyn® Lozenges. The loss of any of these customers could materially and adversely affect our ability to distribute our products, resulting in a negative impact on our operations and financial condition.

We may be unable to accurately estimate demand and monitor wholesaler inventory of Xclair®, Numoisyn® Liquid or Numoisyn® Lozenges. Although we attempt to monitor wholesaler inventory of Xclair®, Numoisyn® Liquid or Numoisyn® Lozenges, we also rely on third party information, which is inherently uncertain and may not be accurate, to assist us in monitoring estimated inventory levels and prescription trends. Inaccurate estimates of the demand and inventory levels of the product may cause our revenues to fluctuate significantly from quarter to quarter and may cause our operating results for a particular quarter to be below expectations.

Inventory levels of Xclair®, Numoisyn® Liquid or Numoisyn® Lozenges held by wholesalers can also cause our operating results to fluctuate unexpectedly. During the year ended December 31, 2008, approximately 85% of our product sales in the United States were to two wholesalers, Cardinal Health, Inc. and McKesson Corp. Inventory levels held by those wholesalers can cause our operating results to fluctuate unexpectedly if our sales to wholesalers do not match end user demand. We have entered into inventory management agreements with these U.S. wholesalers

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under which they provide us with data regarding inventory levels at these wholesalers. However, these wholesalers may not be completely effective in matching inventory levels to end user demand, as they make estimates to determine end user demand. In addition, inventory is held at retail pharmacies and other non-wholesaler locations, for which we have no inventory management agreements and have no control in respect to their buying patterns. Also, the non-retail sector in the United States, which includes government institutions and large health maintenance organizations, tends to be less consistent in terms of buying patterns, and often causes quarter-over-quarter fluctuations in inventory and ordering patterns. We attempt to monitor inventory of Xclair®, Numoisyn® Liquid or Numoisyn® Lozenges in the United States through the use of internal sales forecasts and the expiration dates of product shipped, among other factors. We also rely on third party data to assist us in monitoring estimated pharmacy and other non-wholesaler inventory levels and prescription trends. The information provided by third parties to quantify inventory levels and prescriptions trends is inherently uncertain and may not be accurate. Because the methodology behind the third party information is proprietary, we are unable to quantify why third party estimates of inventory and of prescription trends for Xclair®, Numoisyn® Liquid or Numoisyn® Lozenges may be accurate or inaccurate quarter to quarter.

The commercialization of our products is substantially dependent on our ability to develop effective sales and marketing capabilities.

Our successful commercialization of Xclair® Cream, Numoisyn® Liquid and Numoisyn® Lozenges in the United States will depend on our ability to establish and maintain an effective sales and marketing organization in the United States. We hired trained and deployed additional marketing personnel and a national oncology specialty sales force. We may increase or decrease the size of our sales force in the future, depending on many factors, including the effectiveness of the sales force, the level of market acceptance of Xclair® Cream, Numoisyn® Liquid and Numoisyn® Lozenges and the results of our clinical trials. Prior to our launches of these products, we had never sold or marketed any products.

For our product candidates currently under development, our strategy is to develop compounds through the Phase 2 stage of clinical testing and market or co-promote certain of our drugs on our own. We have limited 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 or devices ourselves or through a strategic alliance, product revenues will suffer, we will incur significant additional losses and our share price will be negatively affected.

We may not be able to obtain approval in Canada to market Numoisyn® Liquid.

Numoisyn® Liquid is currently approved for marketing in the United States and we own the rights to market the drug in Canada. There is no guarantee that we will be able to obtain approval to market Numoisyn® Liquid in Canada and hence market the drug and earn potential sales revenue in Canada.

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 our corporate headquarters.

In October 2000, we entered into a 25-year lease for our research and development facility in Dundee, Scotland. Additionally, we lease approximately 40,500 square feet of space in Bothell, Washington, with monthly payments of approximately $0.1 million. 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 sub-leasing of this facility.

We believe that our existing facilities are adequate to accommodate our business needs.

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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, 2008, 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 2008.

PART II

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

Market Information

Our common stock is traded on the NASDAQ Global Market under the symbol CYCC. 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 Cyclacel as reported by the NASDAQ Global Market:

	High	Low
2008		
Quarter ended March 31, 2008	$ 5.51	$ 2.40
Quarter ended June 30, 2008	$ 3.67	$ 1.66
Quarter ended September 30, 2008	$ 2.00	$ 0.84
Quarter ended December 31, 2008	$ 1.16	$ 0.23
2007		
Quarter ended March 31, 2007	$ 8.64	$ 6.70
Quarter ended June 30, 2007	$ 9.50	$ 6.00
Quarter ended September 30, 2007	$ 6.50	$ 4.33
Quarter ended December 31, 2007	$ 5.93	$ 4.90

Holders of Common Stock

On March 30, 2009, we had approximately 61 registered holders of record of our common stock. On March 27, 2009, the closing sale price of our common stock as reported on the NASDAQ Global Market was $0.40 per share.

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Performance Graph

The following graph and table compare the cumulative total return of our common stock, The NASDAQ Composite Index and NASDAQ Biotechnology Index, as described below, for the period beginning March 27, 2006 (the date we became a public company) and ending December 31, 2008, assuming an initial investment of $100 and the reinvestment of any dividends. We obtained the information reflected in the graph and table from independent sources we believe to be reliable, but we have not independently verified the information.

COMPARISON OF 33 MONTH CUMULATIVE TOTAL RETURN*
Among Cyclacel Pharmaceuticals, Inc., The NASDAQ Composite Index
And The NASDAQ Biotechnology Index

* $100 invested on 3/27/06 in stock & 2/28/06 in index-including reinvestment of dividends.

Fiscal year ending December 31.

Name	March 27, 2006	December 31, 2006	December 31, 2007	December 31, 2008
Cyclacel	100.00	85.86	68.59	5.26
Nasdaq Composite	100.00	107.56	117.24	68.71
NASDAQ Biotechnology	100.00	93.30	94.18	88.44

Performance Graph and related information shall not be deemed soliciting material or to be filed with the Securities and Exchange Commission, nor shall such information be incorporated by reference into any future filing under the Securities Act of 1933 or Securities Exchange Act of 1934, each as amended, except to the extent that the Company specifically incorporates it by reference into such filing.

Dividends

We have never declared nor 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 or accrue quarterly dividend payments on our convertible preferred stock.. Except for dividends we paid 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,

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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 paid dividends during 2008 to the holders of our preferred stock.

Unregistered Sales of Securities

None.

Securities Authorized for Issuance Under Equity Compensation Plans

The following table provides certain aggregate information with respect to all of our equity compensation plans in effect as of December 31, 2008:

Plan Category	(a) No. of Securities to be Issued upon Exercise of Outstanding Options, Warrants and Rights	(b) Weighted-Average Exercise Price of Outstanding Options, Warrants and Rights	(c) Number of Securities Remaining Available for Future Issuance under Equity Compensation Plans (Excluding Securities Reflected in Column (a))
Total equity compensation plans approved by security holders(1)	3,674,899	$ 4.36	1,499,593
Equity compensation plans not approved by security holders			

(1) Consists of our Amended and Restated 2006 Stock Option Plan (the 2006 Plan). The 2006 Plan provides for the grant of incentive stock options, nonqualified stock options, stock appreciation rights, restricted stock and performance units. The number of shares available for issuance, as of March 30, 2009, under the 2006 Plan is 5,200,000.

Item 6. ***Selected Financial Data***

This section presents our historical financial data. The consolidated statement of operations data for the years ended December 31, 2006, 2007 and 2008 and for the period from August 13, 1996 (inception) to December 31, 2008 and the consolidated balance sheet data as of December 31, 2007 and 2008 have been derived from our audited financial statements included elsewhere in this Form 10-K. The statement of operations data for the years ended 2004 and 2005 and the balance sheet data as of December 31, 2004, 2005 and 2006 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.

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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.

	Years Ended December 31,					Period from August 13, 1996 (Inception) to December 31,
	2004	2005	2006	2007	2008	2008
	(In thousands)					
Consolidated Statements of Operations:						
Revenues:						
Collaboration and research and development income	$ 102	$ 245	$ 231	$ 10	$	$ 3,000
Product revenue					838	838
Grant income	823	111	156	119	39	3,635
	925	356	387	129	877	7,473
Operating expenses:						
Cost of goods sold					429	429
Research and development	20,332	15,841	21,205	19,569	18,869	160,413
Selling, general and administrative	3,543	5,264	12,598	12,033	15,354	63,308
Goodwill and intangibles impairment					7,934	7,934
Other restructuring costs			225	1,554	489	2,268
Total operating expenses	23,886	21,131	34,028	33,156	43,075	234,352
Operating loss	(22,961)	(20,775)	(33,641)	(33,027)	(42,198)	(226,879)
Total other (expense) income	(2,248)	801	2,138	6,933	63	7,890
Loss before taxes	(25,198)	(19,948)	(31,503)	(26,094)	(42,135)	(218,989)
Income tax benefit	2,456	1,900	2,245	2,041	1,749	16,274
Net loss	(22,742)	(18,048)	(29,258)	(24,053)	(40,386)	(202,715)

Dividends on preferred shares	(11,053)	(11,876)	(2,827)			(38,123)
Net loss applicable to common shareholders	$ (33,795)	$ (29,924)	$ (32,085)	$ (24,053)	$ (40,386)	$ (240,838)
Net loss per share basic and diluted	$ (5.10)	$ (4.50)	$ (2.40)	$ (1.21)	$ (1.98)	
Shares used in computing basic and diluted net loss per share	6,627,831	6,656,732	13,390,933	19,873,911	20,433,129	

	As of December 31,				
	2004	**2005**	**2006**	**2007**	**2008**
			(In thousands)		
Consolidated Balance Sheet Data:					
Cash and cash equivalents	$ 7,766	$ 3,117	$ 44,238	$ 30,987	$ 24,220
Short-term investments	15,152	10,690	9,764	27,766	1,502
Working capital	20,909	2,152	50,244	49,065	20,386
Total assets	31,176	19,071	63,276	75,912	30,957
Long-term debt, net of current portion	(368)	(78)	(1,436)	(3,231)	(1,688)
Total stockholders equity	23,953	4,119	53,919	57,969	20,642

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In connection with the stock purchase agreement with Xcyte Therapies Inc. or Xcyte in March 2006, 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.

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. Certain 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, 2008 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 diversified biopharmaceutical business dedicated to the discovery, development and commercialization of novel, mechanism- targeted drugs to treat cancer and other serious disorders. Our strategy is focused on leading edge therapeutic management of cancer patients based on a portfolio of three products marketed by our ALIGN subsidiary and a clinical development pipeline. 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 the quality of life and improving survival rates of cancer patients. We have been focused on the cell cycle since our inception. We market directly in the United States Xclair® Cream for radiation dermatitis and Numoisyn® Liquid and Numoisyn® Lozenges for xerostomia.

As a result of the recent revised operating plan announced on September 16, 2008, we are focusing our clinical development priorities on:

Sapacitabine in acute myeloid leukemia or AML in the elderly;

Sapacitabine in myelodysplastic syndromes or MDS;

Sapacitabine in cutaneous T-cell lymphoma or CTCL; and

Sapacitabine in non small-cell lung cancer or NSCLC.

We may continue to fund certain additional programs pending the availability of clinical data, at which time we will determine the feasibility of pursuing advanced development including:

Seliciclib in nasopharyngeal cancer or NPC;

Seliciclib in non small-cell lung cancer; and

CYC116 in patients with solid tumors.

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Our core area of expertise is in cell cycle biology, or the processes by which cells divide and multiply. We focus primarily on the 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 the 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 nucleoside analogues, cyclin dependent kinase or CDK inhibitors and Aurora kinase/Vascular Endothelial Factor Receptor 2 or AK/VEGFR2 inhibitors. Although a number of pharmaceutical and biotechnology companies are currently attempting to develop nucleoside analogues, CDK inhibitor and AK inhibitor drugs, we believe that our drug candidates are differentiated in that they are orally available and interact with unique target profiles and mechanisms. For example we believe that our sapacitabine is the only orally available nucleoside analogue presently being tested in Phase 2 trials in AML and seliciclib is the only orally available CDK inhibitor currently in Phase 2 trials.

We have worldwide rights to commercialize sapacitabine, seliciclib and CYC116 and our business strategy is to enter into selective partnership arrangements with these programs. 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 a research facility located in the United Kingdom.

From our inception in 1996 through December 31, 2008, 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, 2008, our accumulated deficit during the development stage was approximately $202.7 million. We expect to continue incurring substantial losses for the next several years as we continue to develop our clinical and pre-clinical drug candidates. Our operating expenses comprise research and development expenses and selling and general and administrative expenses.

To date, we have not generated significant 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. Prior to October 2007, our revenue consisted of collaboration and grant revenue. Beginning in 2008 we recognized revenue from sales of commercial products, for the first time, following the ALIGN acquisition in October 2007. In accordance with our revenue recognition accounting policy, we did not recognize any revenue from sales of commercial products in 2007. We have recognized revenues from inception through December 31, 2008 totaling approximately $7.5 million of which approximately $3.0 million is derived from fees under collaborative agreements, approximately $3.6 million of grant revenue from various United Kingdom government grant awards and approximately $0.8 million from product sales. We have also recognized amounts receivable from the United Kingdom s tax authority, H.M. Revenue & Customs of $16.3 million for research and development tax credits since inception.

Recent Events

Restructuring expense

In September 2008, we announced a revision of our operating plan that concentrates our resources on the advancement of our lead drug, sapacitabine, while maintaining our core competency in drug discovery and cell cycle biology. The plan reduced the workforce across all locations by 25 people or approximately 30%. We recorded approximately $0.4 million for severance payments and $0.1 million of accelerated depreciation for assets that will no longer be utilized. All severance payments were paid as of December 31, 2008. We assigned the lease of our redundant

Cambridge research facility back to the landlord and, in accordance with the terms of the lease, will incur a net charge, incorporating a surrender fee, of $0.1 million to effect this.

Goodwill and intangible asset impairment

In September 2008, the goodwill acquired in the Xcyte transaction was written down in full and we recorded an impairment charge of approximately $2.7 million in accordance with FAS No. 142, *Goodwill and Other Intangible*

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Assets (FAS 142). This impairment charge was triggered primarily by a decline in our stock price that reduced our market capitalization below book value of the net assets of Xcyte. Our reduced market capitalization reflected the general decline in the economic environment.

Intangible assets acquired in the ALIGN transaction were also fully written down in September 2008, in accordance with FAS No. 144, *Accounting for the Impairment or Disposal of Long-Lived Assets,* (FAS 144). An impairment charge of approximately $3.6 million was identified and recognized in the consolidated statement of operations. This one-time charge was triggered by a downward revision of projected net cash flows from product sales, required due to budgetary constraints experienced by health care providers and restrictions of the cost reimbursement program. As a result the sum of the expected undiscounted cash flows was less than the carrying amount of the intangible assets on September 30, 2008.

In December 2008, goodwill allocated to our ALIGN reporting unit following the ALIGN acquisition was fully written down in accordance with FAS 142, resulting in an impairment charge of approximately $1.6 million being recognized on the consolidated statement of operations. Further decline in our stock price during the fourth quarter of 2008 caused us to perform an impairment analysis during December 2008. In determining the impairment charge, we considered the negative impact the current economic situation might have on sales growth expectations of the ALIGN products resulting in a downward revision of projected net cash flows from product sales. These factors caused the discounted cash flows for the reporting unit to be less than its carrying value on December 31, 2008.

Acquisition of ALIGN Pharmaceuticals, LLC and ALIGN Holdings, LLC

On October 5, 2007, Achilles Acquisition, LLC renamed immediately following the acquisition to ALIGN Pharmaceuticals, LLC, or ALIGN, a wholly-owned subsidiary of Cyclacel, entered into an asset purchase agreement with ALIGN Pharmaceuticals, LLC and ALIGN Holdings, LLC or Sellers, to acquire substantially all of the Sellers assets. The transaction closed on the same date.

We acquired the Sellers exclusive rights to sell and distribute three products in the United States used potentially to manage the effects of radiation or chemotherapy in cancer patients: Xclair® Cream, Numoisyn® Liquid and Numoisyn® Lozenges. The acquired business provides us with the foundation to build a commercial organization focused on cancer that is complementary to our oncology/hematology products in development and is part of our strategy to build a diversified biopharmaceutical business.

Under the terms of the asset purchase agreement, we (i) paid approximately $3.3 million in cash to the Sellers at closing, plus approximately $0.5 million to pay certain creditors of the Sellers, (ii) committed to make future payments of approximately $0.6 million in 2009 and $0.6 million in 2010 as part of securing long term supply arrangements and (iii) agreed to issue up to a maximum aggregate of 184,176 shares of our common stock, or the Stock Consideration, as consideration for the asset purchase. 46,044 shares of the Stock Consideration were issuable on the first anniversary of the closing date, and the balance was issuable in two tranches upon achievement of certain operational and financial milestones (in all cases, subject to satisfaction of any outstanding indemnification obligations of the Sellers). The Sellers failed to meet the financial milestones and forfeited 46,044 and 92,088 shares of our common stock on April 5, 2008 and on December 31, 2008, respectively. In addition, pursuant to an indemnity clause in the asset purchase agreement, one or more Events of Indemnification (as defined in the agreement) occurred entitling us to set off certain claims against our common stock which would have otherwise been issuable on October 5, 2008, the first anniversary of the closing date. Our claims were in excess of the stock consideration and the Sellers forfeited the entire payment of 46,044 shares. The final purchase price was reduced to reflect the equity forfeited by the Sellers, with a reduction to the goodwill recognized on acquisition.

The transaction was accounted for as a business combination and the consolidated results of operations of the Company included the results of operations of the Sellers from the closing date. The assets and certain agreed liabilities of ALIGN were recorded as of the closing date at their estimated fair values.

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Acquisition Final Purchase Price

The final purchase price to acquire the Sellers assets was calculated as follows (in thousands):

Cash	$ 3,331
Acquisition costs	432
Total purchase price	$ 3,763

Acquisition Final Purchase Price Allocation

As part of the acquisition, we acquired the following net assets (in thousands):

Current assets	$ 199
Property, plant and equipment	10
Intangible assets	4,495
Current liabilities	(1,409)
Non-current liabilities	(1,122)
Goodwill	1,590
	$ 3,763

Results of Operations

In connection with the stock purchase agreement Xcyte in March 2006, 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.

In connection with the asset purchase agreement with ALIGN, Cyclacel recorded the assets and liabilities of ALIGN at fair value on October 5, 2007. The results of operations and balance sheet data for 2007 reflect the results of the combined companies from October 5, 2007 through December 31, 2007.

Years ended December 31, 2007 and 2008 compared to years ended December 31, 2006 and 2007, respectively.

Revenues

The following table summarizes the components of our revenues for the years ended December 31, 2006, 2007 and 2008:

	Years Ended December 31,	**$ Differences**	**% Differences**

	2006	2007	2008	2006 to 2007	2007 to 2008	2006 to 2007	2007 to 2008
	(In thousands)						
Collaboration and research and development revenue	$ 231	$ 10	$	$ (221)	$ (10)	(96)%	(100)%
Product Revenue			838		838		100%
Grant revenue	156	119	39	(37)	(80)	(24)%	(67)%
Total revenue	$ 387	$ 129	$ 877	$ (258)	$ 748	(67)%	580%

Collaboration and research and development revenue is derived from several agreements under which the Company provides compounds for evaluation for an agreed consideration. The majority of these arrangements ceased during 2006, resulting in the reduction of 96% from approximately $0.2 million in the year ended December 31, 2006 to $10,000 in the year ended December 31, 2007. No revenue was recognized under collaborative agreements during 2008.

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Product revenue is derived from the sale of Xclair® Cream, Numoisyn® Liquid and Numoisyn® Lozenges following the ALIGN asset acquisition on October 5, 2007. During the year ended December 31, 2008, we recognized product revenue for the first time, in accordance with our revenue recognition policy, of approximately $0.8 million.

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. Grant revenue decreased by 24% from approximately $0.2 million in the year ended December 31, 2006 to approximately $0.1 million in the year ended December 31, 2007 and by 67% from $0.1 million in 2007 to approximately $39,000 in 2008. This is as a direct result of our progressing projects past qualifying research to a later stage which does not attract grant funding, and a reduction in expenditure directed at qualifying research programs.

The future

This was the first full year of ALIGN product sales, reflecting our relaunch of the three products since we acquired ALIGN. We expect to continue to grow the business and sales of ALIGN products in 2009 as a result of our continued investment in sales force infrastructure and marketing efforts.

Cost of goods sold

	Years Ended December 31,			$ Differences		% Differences	
	2006	2007	2008	2006 to 2007	2007 to 2008	2006 to 2007	2007 to 2008
			(In thousands)				
Cost of goods sold	$	$	$ 429	$	$ 429	%	100%

Total cost of sales represented 51% of product revenue for the year ended December 31, 2008. We expect that as volumes of product sales increase, cost of sales as a percentage of product sales will reduce as the fixed element of distribution costs is allocated across an increased numbers of products sold.

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 sapacitabine, seliciclib and CYC116, the advancement of product candidates toward clinical and pre-clinical trials and the development of in-house research to advance our biomarker program and technology platforms. During 2008, in response to changing market conditions, we reduced then stopped expenditure on development and preclinical activities outside of our core projects. We expense all research and development costs as they are incurred. Research and development expenses primarily include:

- clinical trial and regulatory-related costs;
- payroll and personnel-related expenses, including consultants and contract research;
- preclinical studies and laboratory supplies and materials;

technology license costs; and

rent and facility expenses for our laboratories.

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The following table provides information with respect to our research and development expenditure for the years ended December 31, 2006, 2007 and 2008:

	Years Ended			$ Differences		% Differences	
	2006	2007	2008	2006 to 2007	2007 to 2008	2006 to 2007	2007 to 2008
	(In thousands)						
Sapacitabine	$ 1,841	$ 3,326	$ 6,601	$ 1,485	$ 3,275	81%	98%
Seliciclib	3,126	3,270	2,906	144	(364)	5%	(11)%
CYC116	6,712	2,626	1,695	(4,086)	(931)	(61)%	(35)%
Other costs related to research and development programs, management and exploratory research	9,526	10,347	7,667	821	(2,680)	9%	(26)%
Total research and development expenses	$ 21,205	$ 19,569	$ 18,869	$ (1,636)	$ (700)	(8)%	(4)%

Research and development expenses represented 62%, 59% and 44% of our operating expenses for the years ended December 31, 2006, 2007 and 2008 respectively. Included in research and development expense is stock-based compensation of approximately $6.2 million, $0.8 million and $0.7 million for the years ended December 31, 2006, 2007 and 2008, respectively.

Fiscal 2008 as compared to fiscal 2007. Research and development costs decreased by 4% or approximately $0.7 million from approximately $19.6 million for the year ended December 31, 2007 to approximately $19.0 million for the year ended December 31, 2008. The sapacitabine program increased by approximately $3.3 million relating to the increased clinical trial activities, in particular the commencement of the Phase 2 trial in elderly AML in December 2007, the expansion of the trial to explore myelodysplastic syndromes, as well as additional pre-clinical and product scale-up. This has been offset by cost reductions in other programs and cost savings from the workforce reduction in September 2008 to allow us to concentrate on the advancement of sapacitabine. The increase in strength of the U.S. dollar against the British Pound has also contributed to lower research and development expenses being recognized on the consolidated statement of operations for the year ended December 31, 2008 as compared to the year ended December 31, 2007.

Fiscal 2007 as compared to fiscal 2006. Research and development costs decreased 8% or approximately $1.6 million from approximately $21.2 million for the year ended December 31, 2006 to approximately $19.6 million for the year ended December 31, 2007. Significant components of the change relate to a decrease in the charge for stock-based compensation of approximately $5.4 million from $6.2 million during 2006 to $0.8 million during 2007 as a result of the stock options granted during June 2006 being two-thirds vested immediately upon grant. This decrease was offset by an increase in costs of approximately $1.6 million related to sapacitabine and seliciclib as we increased the number of Phase 2 trials in 2007. Additionally, CYC116 expenses decreased by approximately $4.1 million from approximately $6.7 million for the year ended December 31, 2006 to approximately $2.6 million for

the same period in 2007. The decreases in expenses were attributable to the CYC116 program being in full pre-clinical studies during 2006 and then moving to a Phase 1 study in 2007.

The future

In September 2008, we announced a revision of our operating plan to concentrate on the advancement of our lead drug sapacitabine and to reduce our research and development costs in the other core programs to maximize the benefit of our available cash resources. We expect that the full benefit of this revision will be realized in 2009.

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Selling, general and administrative expenses

Selling, general and administrative expenses include costs for sales and marketing operations, administrative personnel, legal and other professional expenses and general corporate expenses. The following table summarizes the total selling, general and administrative expenses for the years ended December 31, 2006, 2007 and 2008:

	Years Ended			$ Differences		% Differences	
	2006	2007	2008	2006 to 2007	2007 to 2008	2006 to 2007	2007 to 2008
Total selling, general and administrative expenses	$ 12,598	$ 12,033	$ 15,354	$ (565)	$ 3,321	(4)%	28%

Total selling, general and administrative expenses represented 37%, 36% and 36% of our operating expenses for the years ended December 31, 2006, 2007 and 2008, respectively.

Fiscal 2008 as compared to fiscal 2007. Selling, general and administrative expenditure increased 28% or $3.3 million to approximately $15.3 million for the year ended December 31, 2008 from approximately $12.0 million for the year ended December 31, 2007, primarily attributable to the sales operations of ALIGN. Included within the expense of $15.3 million for the year ended December 31, 2008 are approximately $2.3 million of costs in respect of the support and development of ALIGN s commercial operations and sales and marketing, reflecting the fact that 2008 is the first full year of reporting for the ALIGN business following its acquisition in October 2007. In addition, $0.7 million of intangible asset amortization charges were recognized prior to the intangible asset impairment. Included in selling, general and administrative expenses is stock compensation of approximately $0.9 million and $1.0 million for the years ended December 31, 2007 and 2008 respectively.

Fiscal 2007 as compared to fiscal 2006. Selling, general and administrative expenditure decreased 4% or approximately $0.6 million from $12.6 million in the year ended December 31, 2006 to $12.0 million in the year ended December 31, 2007. The reduction in expenses was primarily attributable to a decrease in the stock based compensation of approximately $2.5 million from $3.4 million during 2006 to $0.9 million during 2007. This was offset by sales and marketing expenditure of approximately $0.8 million related to the new ALIGN acquisition as well as Delaware taxation, recruitment costs, legal costs which increased by $0.2 million, respectively.

The future

Further to the increase in our selling, general and administrative expenses recorded in 2008 following our acquisition of ALIGN, we expect our selling, general and administrative expenses remain at similar levels to 2008 in the coming year.

Goodwill and intangible asset impairment

The following table summarizes the goodwill and intangibles impairment charges for years ended December 31, 2006, 2007 and 2008:

	Years Ended			$ Differences		% Differences	
	2006	2007	2008	2006 to 2007	2007 to 2008	2006 to 2007	2007 to 2008
	(In thousands)						
Goodwill and intangibles impairment			$ 7,934		$ 7,934		100%

In September 2008, the goodwill acquired in the Xcyte transaction was written down in full and we recorded an impairment charge of approximately $2.7 million in accordance with FAS 142. This impairment charge was identified through our annual impairment review process and was triggered primarily by a decline in our stock price that reduced our market capitalization below book value of the net assets of the Xcyte reporting unit. Our reduced market capitalization reflected the general decline in the economic environment.

Intangible assets acquired in the ALIGN transaction were also fully written down in September 2008, in accordance with FAS 144. An impairment charge of approximately $3.6 million was identified through our annual impairment review process and was recognized on the consolidated statement of operations. This one-time non-

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cash charge was triggered by a downwards revision of our projected net cash flows from product sales, required due to budgetary constraints experienced by health care providers and restrictions of the cost reimbursement regime. As a result, the sum of the expected undiscounted cash flows was less than the carrying amount of the intangible assets on September 30, 2008.

In December 2008, goodwill allocated to our ALIGN reporting unit following the ALIGN acquisition was fully written down in accordance with FAS 142, resulting in an impairment charge of approximately $1.6 million being recognized on the consolidated statement of operations. A further decline in our stock price during the fourth quarter of 2008 caused us to perform an impairment analysis during December 2008. In determining the impairment charge, we considered the negative impact the current economic situation might have on sales growth expectations of the ALIGN products resulting in a downward revisions of projected net cash flows from product sales. These factors caused the discounted cash flows for the reporting unit to be less than its carrying value on December 31, 2008.

The future

Previously recognized goodwill and intangible assets acquired have been fully impaired as of December 31, 2008.

Restructuring charge

The following table summarizes the restructuring charges for years ended December 31, 2006, 2007 and 2008:

	Years Ended			$ Differences		% Differences	
	2006	2007	2008	2006 to 2007	2007 to 2008	2006 to 2007	2007 to 2008
	(In thousands)						
Total restructuring charge	$ 225	$ 1,554	$ 546	$ 1,329	$ (1,008)	591%	(65)%

Fiscal 2008 as compared to fiscal 2007. The restructuring charge decreased by 65% or $1.0 million from approximately $1.5 million for the year ended December 31, 2007 to $0.5 million for the year ended December 31, 2008.

In September 2008, we announced a revision of our operating plan that concentrates our resources on the advancement of our lead drug, sapacitabine, while maintaining a core competency in drug discovery and cell cycle biology. The plan reduced the workforce across all locations by 25 people. We recorded and paid approximately $0.4 million of severance costs and $0.1 million of accelerated depreciation for assets that will no longer be utilized. In addition we have accrued a charge of $0.1 million in respect of costs of exiting the lease of our redundant Cambridge research facility.

During the year ended December 31, 2008 there were no changes to the assumption and estimates underlying the restructuring liability associated with exiting the Bothell facility. As of December 31, 2008, the fair value of the remaining lease payments, net of estimated sub-lease income was $2.1 million.

Fiscal 2007 as compared to fiscal 2006. In March 2006, we 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, we 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 increase to the restructuring provision in the third quarter of 2006 of $0.2 million in recognition of commissions payable upon successful conclusion of a sublease agreement.

For the year ended December 31, 2007, a charge of approximately $1.6 million was recognized in the consolidated statement of operations to reflect the reduced likelihood of any sublet income as a result of a further deterioration in the commercial real estate market conditions in the Bothell area.

The future

As of December 31, 2008, the restructuring liability associated with exiting the Bothell facility was approximately $2.1 million representing the present value of the remaining lease payments, net of estimated

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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 adjust the accrual if necessary. These changes may be material.

As a result of the workforce reduction in September 2008, we will vacate our laboratory facility in Cambridge, England. We assigned the lease of our redundant Cambridge research facility back to the landlord and, in accordance with the terms of the lease, will incur a net charge, incorporating a surrender fee, of $0.1 million to effect this. The need for further revisions to our operating plan may be required and will be assessed as circumstances dictate.

Other income

The following table summarizes the other income for years ended December 31, 2006, 2007 and 2008:

	Years Ended			$ Differences		% Differences	
	2006	2007	2008	2006 to 2007	2007 to 2008	2006 to 2007	2007 to 2008
			(In thousands)				
Change in valuation of derivative	$ (215)	$ (93)	$	$ 122	$ 93	(57)%	(100)%
Change in valuation of warrants liability		3,205	3,502	3,205	$ 297		9%
Foreign Exchange gain/(loss)	279	490	(4,501)	211	(4,991)	76%	(1019)%
Interest income	2,328	3,554	1,380	1,226	(2,174)	53%	(61)%
Interest expense	(254)	(223)	(318)	31	(95)	(12)%	42%
Total other income, net	$ 2,138	$ 6,933	$ 63	$ 4,795	$ (6,870)	224%	(99)%

Fiscal 2008 as compared to fiscal 2007. Total other income, net, reduced by approximately $6.9 million from $6.9 million in 2007 to $63,000 in 2008. The most significant impact is the movement in foreign exchange gains and losses with a negative impact of $5.0 million. This is due to the significant increase in the strength of the United States dollar against the British pound as further detailed below.

On November 3, 2007, the embedded derivative associated with the dividend make-whole payment expired reducing the liability to $0 and thus no further marked to market adjustments will be made with regard to this embedded derivative.

The change in valuation of warrants relates to the issue of warrants to purchase shares of our common stock under the registered direct financing completed in February 2007. The warrants issued to the investors meet the requirements of and are being accounted for as a liability in accordance with EITF 00-19 *Accounting for Derivative Financial Instruments Indexed to, and Potentially Settled in, a Company s Own Stock.* or EITF 00-19. The value of the warrants is being marked to market each reporting period as a derivative gain or loss until exercised or expiration. For the years ended December 31, 2007 and 2008, we recognized the change in the value of warrants of approximately $3.2 million and $3.5 million, respectively, as other income in the consolidated statement of operations.

During the year ended December 31, 2008 there were unfavorable unrealized foreign exchange movements of approximately $17.2 million on intercompany loans due to the increase in the strength of the United States dollar against the British pound. Of this, $4.8 million is recorded in the consolidated statement of operations within the separate line item foreign exchange gains/(losses), within other income (expense). This has been offset by a realized gain of $0.3 million on transactions in the year in respect of underlying operations, resulting in a net foreign exchange loss of $4.5 million.

In conjunction with the operational review conducted by the Company in September 2008, the nature of intercompany funding was considered. It was concluded that as repayment of intercompany loans is not expected in the foreseeable future, the nature of the funding advanced was of a long-term investment nature and that the terms of the loans should be amended to reflect this. Effective October 1, 2008 intercompany loans ceased to be repayable on demand and have no fixed repayment date. As a result of the change in repayment terms, from October 1, 2008 all

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unrealized foreign exchange gains or losses arising on intercompany loans are recognized in other comprehensive income. This has restricted the unfavorable unrealized foreign exchange movements recorded in other income to $4.8 million, with $12.3 million recognized in other comprehensive income for the three months from October 1, 2008 to December 31, 2008. Future unrealized foreign exchange gains or losses arising on the intercompany loans will be recognized in other comprehensive income on the consolidated statement of stockholders equity until repayment of the intercompany loan becomes foreseeable.

Prior year foreign exchange gains of $0.3 million and $0.5 million for the years ended December 31, 2006 and 2007 respectively, have been reclassified to other income (expense) from selling, general and administrative expense for comparative purposes.

Interest income decreased by approximately $2.2 million from $3.6 million for the year ended December 31, 2007 to $1.4 million for the year ended December 31, 2008. During 2008, maturing short-term investments were reinvested in cash and cash equivalents, being a more secure form of investment and providing greater liquidity. As a result, these assets attracted a lower rate of interest. This was compounded by a reduction in the average balance of cash and cash equivalents and short-term investments during 2008 as compared to 2007.

Interest expense increased by $0.1 million to $0.3 million for the year ended December 31, 2008 from $0.2 million for year ended December 31, 2007. For each of the years ended December 31, 2007 and 2008, we recorded accretion expense associated with the Bothell restructuring lease of $0.2 million on the consolidated statement of operations as interest expense. A further $0.2 million of accretion expense will be recognized over the remaining life of the lease to December 2010. During the year ended December 31, 2008, interest associated with notes payable in relation to the acquisition of ALIGN on October 5, 2007 of approximately $0.1 million was also recognized.

Fiscal 2007 as compared to fiscal 2006. Total other income, net, increased by approximately $4.8 million to $6.9 million in 2007 from $2.1 million in 2006.

The change in derivative value of $0.2 million and $0.1 million for the years ended December 31, 2006 and 2007 respectively is associated with the dividend make-whole payment on our outstanding convertible exchangeable preferred stock. The dividend make-whole feature of the convertible exchangeable preferred stock expired on November 3, 2007.

The change in valuation of warrants liability relates to the issue of warrants to purchase shares of common stock under the registered direct financing completed in February 2007. There were no outstanding warrants requiring to be marked to market in the year ended December 31, 2006.

The increase in interest income of approximately $1.2 million to approximately $3.6 million for the year ended December 31, 2007 from $2.3 million for the year ended December 31, 2006, is primarily attributable to higher average balances of cash and cash equivalents and short-term investments in 2007 as a result of the receipt of $33.4 million in net proceeds from the registered direct financing described above.

Interest expense for the year ended December 31, 2007 decreased by 12% from the year ended December 31, 2006. During 2006 interest expenses resulted primarily from interest associated with a government loan, the principal of which was repaid in the fourth quarter of 2006. During 2007 interest expense resulted primarily from accretion expense associated with the Bothell lease restructuring provision which amounted to approximately $0.2 million.

The future

The valuation of the warrant liability will continue to be re-measured at the end of each reporting period. The valuation of the warrants is dependent upon many factors, including our stock price, interest rates and the remaining term of the instrument and may fluctuate significantly, which may have a significant impact on our statement of operations.

As the nature of funding advanced through inter-company loans is that of a long-term investment in nature, future unrealized foreign exchange gains and losses on such funding will be recognized in other comprehensive

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income until repayment of the intercompany loan becomes foreseeable. This will minimize the future impact of unrealized foreign exchange fluctuations on earnings.

A further accretion expense of approximately $0.2 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, 2006, 2007 and 2008:

	Years Ended			$ Differences		% Differences	
	2006	2007	2008	2006 to 2007	2007 to 2008	2006 to 2007	2007 to 2008
	(In thousands)						
Total income tax benefit	$ 2,245	$ 2,041	$ 1,749	$ (204)	$ (292)	(9)%	(14)%

Fiscal 2008 as compared to fiscal 2007. Research and development tax credits recoverable decreased by 14% or approximately $0.3 million from approximately $2.0 million for the year ended 2007 to approximately $1.7 million for the year ended December 31, 2008. The level of tax credits recoverable is linked directly to qualifying research and development expenditure incurred in any one year but restricted to payroll taxes paid by us in the United Kingdom in that same year. The decrease was a reflection of decreased income taxes available for recovery as a consequence of the lower eligible research and development payroll expenses in the United Kingdom in 2008 following the workforce reductions announced in September 2008.

Fiscal 2007 as compared to fiscal 2006. Research and development tax credits recoverable decreased 9% or $0.2 million from $2.2 million in 2006 to $2.0 million in 2007. The level of tax credits recoverable is linked directly to qualifying research and development expenditure incurred in any one year but restricted to payroll taxes paid by us in that same year. This decrease was a reflection of the higher income taxes available to recover in 2006 compared to 2007 from the payroll 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.

The 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, however as a result of our revised operating plan announced in September 2008 the amount of payroll taxes payable in future periods will be lower than in previous periods, restricting available income tax credits to that lower amount.

Liquidity and Capital Resources

The following is a summary of our key liquidity measures as at December 31, 2007 and 2008:

	December 31, 2007	December 31, 2008	$ Difference	% Difference
		(In thousands)		
Cash and cash equivalents	$ 30,987	$ 24,220	$ (6,767)	(22)%
Short-term investments, available for sale	27,766	1,502	(26,264)	(95)%
Total cash and cash equivalents and short-term investments	$ 58,753	$ 25,722	$ (33,031)	(56)%
Current assets	$ 63,777	$ 29,014	$ (34,763)	(55)%
Current liabilities	14,712	8,624	(6,088)	(41)%
Working capital	$ 49,065	$ 20,390	$ (28,675)	(58)%

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At December 31, 2008, we had cash and cash equivalents and short-term investments of $25.7 million as compared with $58.8 million at December 31, 2007. The February 2007 registered direct financing of $33.4 million in net proceeds is reflected in the balance at December 31, 2007, and the lower balance at December 31, 2008 was primarily due to funding ongoing clinical trials, research and development and to a lesser extent sales and marketing activities.

Current liabilities reduced by 41% or $6.1 million from $14.7 million as at December 31, 2007 to $8.6 million as at December 31, 2008. $3.5 million of this reduction relates to the reduction in the fair value of warrants to purchase shares of our common stock which were issued under the registered direct financing completed in February 2007, as these warrants are marked to market at every reporting date. In addition, the current liabilities balance of $15.0 million as at December 31, 2007 included one-off accounts payable balances in respect of purchases of property, plant and equipment of approximately $0.9 million and amounts payable to certain creditors for the manufacture of our drugs for use in clinical trials of approximately $0.9 million.

Since our inception, we have not generated any significant product revenues 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, 2008, we had an accumulated deficit of $202.7 million.

We believe that existing funds together with cash generated from operations and potential financing activities are sufficient to satisfy our planned working capital, capital expenditures, debt service and other financial commitments for at least the next twelve months. Current business and environmental risks could have a detrimental affect on the availability of sources of funding and our ability to access them in the future.

Cash provided by (used in) operating, investing and financing activities

Cash provided by (used in) operating, investing and financing activities for the years ended December 31, 2006, 2007 and 2008 is summarized as follows:

	Year Ended December 31,		
	2006	2007	2008
	(In thousands)		
Net cash used in operating activities	$ (20,172)	$ (23,140)	$ (29,905)
Net cash provided by (used by) investing activities	$ 3,911	$ (22,693)	$ 27,342
Net cash provided by (used by) financing activities	$ 57,400	$ 32,208	$ (1,238)

Fiscal 2008 as compared to fiscal 2007.

Operating activities

Net cash used in operating activities increased by $6.8 million, to $29.9 million in 2008 from $23.1 million in 2007. Net cash used in operating activities during the year ended December 31, 2008 of $29.9 million resulted from our net operating loss of $40.4 million, adjusted for material non-cash activities comprising amortization of investment premiums (discounts), change in valuation of liability-classified warrants, depreciation and amortization, goodwill and

intangibles impairment, unrealized foreign exchange losses and non-cash stock based compensation expense, amounting to $11.4 million and a net reduction in working capital of $0.9 million due to a decrease in prepaid expenses combined with a net decrease in accounts payable and other current liabilities.

Net cash used in operating activities during 2007 of $23.1 million resulted primarily from our net loss of $24.1 million, adjusted for material non-cash activities comprising amortization of investment premiums (discounts), change in valuation of derivative, change in valuation of liability-classified warrants, depreciation and amortization, non-cash stock based compensation expense and provision for restructuring costs, amounting to $1.7 million and net increase in working capital of $1.2 million due to an decrease in prepaid expenses combined with a net increase in accounts payable and accrued expenses.

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The increase of $6.8 million in net cash used in operations was mainly due to additional expenditure on the development of the ALIGN business, a reduction in interest earned, restructuring costs incurred during the year, a reduction in research and development tax credits received and the year on year change in working capital.

Investing activities

Net cash used in investing activities in the year ended December 31, 2007 amounted to $22.7 million. During the year ended December 31, 2008, cash provided by investing activities amounted to $27.3 million. During the year ended December 31, 2007, we purchased short-term investments totalling $153.6 million which was offset by maturities of $136.4 million in short term investments and incurred cash expenditures of $3.8 million for the acquisition of ALIGN on October 5, 2007. During 2008, the proceeds from maturing short-term investments were reinvested in cash and cash equivalents to reduce our risk profile. In addition, the net proceeds from $27.7 million of maturing short-term investments were used to fund our operating activities

Capital spending is required to support our research and development initiatives and to maintain our operational capabilities. During the year ended December 31, 2007 and 2008 we invested $1.8 million and $0.4 million, respectively, of cash in key laboratory equipment for research and development purposes.

Financing activities

Net cash provided by financing activities decreased by $33.4 million, from a source of $32.2 million for the year ended December 31, 2007 to a use of $1.2 million for the year ended December 31, 2008.

For the year ended December 31, 2008, the net cash outflow for financing activities primarily related to the payment of our preferred stock dividend of $1.2 million. For year ended December 31, 2007, the net cash provided by financing activities related primarily to net proceeds received from the registered direct financing of $33.4 million in February 2007, offset by payment of our preferred stock dividend of $1.2 million.

Net cash provided by financing activities decreased $25.2 million, from $57.4 million for the year ended December 2006 to $32.2 million. During 2007 the net cash provided by financing activities related primarily to gross proceeds received from the registered direct financing which raised $36.0 million in gross proceeds, before deducting placement agent fees and offering expenses of $2.6 million. During 2006, we received net proceeds of $42.6 million from the April 2006 private placement of common stock and common stock purchase warrants, and assumed $18.0 million of cash and cash equivalents through the Xcyte transaction.

In February 2007 we sold approximately 4.2 million units, each unit consisting of one share of our common stock and a seven-year warrant to purchase 0.25 shares of our common stock, at a purchase price of $8.47125 per unit in a registered direct offering. The purchase price for the shares and the exercise price for the warrants was $8.44 per share, the closing bid price for our common stock on February 12, 2007. Investors paid $0.125 per warrant. We issued 4,249,668 shares of common stock and warrants to purchase 1,062,412 shares of common stock. As of December 31, 2007 and December 31, 2008, the warrants issued to the investors were classified as a liability in accordance with EITF 00-19. At the date of the transaction, the fair value of the warrants of $6.8 million was determined utilizing the Black-Scholes option pricing model utilizing the following assumptions: risk free interest rate 4.58%, expected volatility 85%, expected dividend yield 0%, and a remaining contractual life of 6.88 years. The value of the warrants is being marked to market each reporting period as a derivative gain or loss until exercised or expiration. At December 31, 2007, fair value of the warrants was $3.5 million and at December 31, 2008 the fair value was approximately $43,000. During 2007 and 2008, we recognized a change in the value of warrants of approximately $3.2 million and $3.5 million respectively as a gain on the consolidated statement of operations.

On December 10, 2007, we entered into the committed equity financing facility, or CEFF, with Kingsbridge, in which Kingsbridge committed to purchase the lesser of 4,084,590 shares of common stock or $60 million of common stock from us of capital during the next three years. Under the terms of the agreement, we will determine the exact timing and amount of any CEFF financings, subject to certain conditions. All amounts drawn down under the CEFF will be settled via the issuance of our common stock. We may access capital under the CEFF in tranches as described below, with each tranche being issued and priced over an eight-day pricing period.

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Kingsbridge will purchase shares of common stock pursuant to the CEFF at discounts ranging from 6% to 10% depending on the average market price of the common stock during the eight-day pricing period, provided that the minimum acceptable purchase price for any shares to be issued to Kingsbridge during the eight-day period is determined by the higher of $2.50 or 90% of our common stock closing price the day before the commencement of each draw down.

As of December 31, 2008 we have not drawn down any funds under the CEFF. Since June 16, 2008, we have been unable to draw down any amounts under the CEFF as the closing price of our common stock did not exceed $2.50 per share.

The capital under the CEFF may be accessed in tranches of either (a) 2% of our market capitalization at the time of the draw down or (b) the lesser of (i) 3% of our market capitalization at the time of the draw down and (ii) an alternative draw down amount based on the product of (A) the average trading volume of the 30-day trading period preceding the draw down excluding the five highest and five lowest trading days during such period, (B) the volume-weighted average trading price or VWAP on the trading day prior to the notice of draw down, (C) the number of days during the draw down period and (D) 85%, subject to certain conditions.

In connection with the CEFF, we issued a warrant to Kingsbridge to purchase up to 175,000 shares of common stock at an exercise price of $7.17 per share which represents a 30% premium over the average of the closing bid prices of our common stock during the 5 trading days preceding the signing of the agreement. The warrant became exercisable six months from the date of the agreement and remains exercisable, subject to certain exceptions, for a period of five years thereafter. As of December 31, 2007 and December 31, 2008, the warrants issued to the investors are classified as equity in accordance with EITF 00-19.

Operating Capital and Capital Expenditure Requirements

We expect to continue to incur substantial operating losses in the future. While we have generated modest product revenues from ALIGN product sales for the year ended December 31, 2008, we can not guarantee that we will generate any significant product revenues 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 and short-term investments 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 in the longer term.

We can not 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

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financings or strategic collaborations. Although we are not reliant on institutional credit finance and therefore not subject to debt covenant compliance requirements or potential withdrawal of credit by banks, the current economic climate has also impacted the availability of funds and activity in equity markets. 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 may have to delay, reduce the scope of or eliminate one or more of our clinical trials or research and development programs or make changes to our operating plan similar to the revision made in September 2008. 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.

Off-Balance Sheet Arrangements

As of December 31, 2008, we had no off-balance sheet arrangements.

Critical Accounting Policies

Our discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. Our significant accounting policies are described in Note 2 of the consolidated financial statements. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities and expenses and related disclosure of contingent assets and liabilities. We review our estimates on an ongoing basis. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. Actual results may differ from these estimates under different assumptions or conditions. We believe the judgments and estimates required by the following accounting policies to be critical in the preparation of our consolidated financial statements.

Revenue Recognition

Product sales

We have adopted the following revenue recognition policy related to the sales of Xclair® Cream, Numoisyn® Liquid and Numoisyn® Lozenges. We recognize revenue from these product sales when persuasive evidence of an arrangement exists; delivery has occurred or services have been rendered; the price is fixed and determinable; and collectability is reasonably assured.

As we offer a general right of return on these product sales, we must consider the guidance in FAS No. 48, *Revenue Recognition When Right of Return Exists* (FAS 48) and Staff Accounting Bulletin No. 104 *Revenue Recognition* (SAB 104). Under these pronouncements, we account for all product sales using the sell-through method. Under the sell-through method, revenue is not recognized upon shipment of product to distributors. Instead, upon the shipment of product to distributors, we record deferred revenue at gross invoice sales price, and classify the inventory held by the distributors as deferred cost of sales at the carrying value of the relevant inventory. We recognize revenue when such inventory is sold through to the end user based upon prescriptions filled. To estimate product sold through to end users, we rely on third-party information, including information obtained from significant distributors with respect to their inventory levels and sell-through to customers, and third-party market research data.

Trade Accounts Receivable and Allowance for Doubtful Accounts

Our process for determining the appropriate level of allowance for doubtful accounts involves judgment, and considers the age of the underlying receivables, type of payer, historical and projected collection experience, and current economic and business conditions that could affect the collectability of our receivables. The allowance for

doubtful accounts is reviewed for adequacy, at a minimum, on a quarterly basis. An account is written-off against the allowance for doubtful accounts when reasonable collection efforts have been unsuccessful and it is probable the receivable will not be recovered.

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Changes in the allowance for doubtful accounts are recorded as an adjustment to bad debt expense within general and administrative expenses. Material revisions to reserve estimates may result from adverse changes in collection experience.

Stock-based Compensation

We grant stock options, restricted stock units and restricted stock to officers, employees, directors and consultants under our 2006 Amended and Restated 2006 Equity Incentive Plan, which was amended and restated as of April 14, 2008. We also have outstanding options under various stock-based compensation plans for employees and directors. These plans are described more fully in Note 14 *Stock-Based Compensation Arrangements* .

On January 1, 2006, we adopted FAS 123R using the modified prospective application method. FAS 123R requires measurement of compensation cost for all stock-based awards at fair value on date of grant and recognition of compensation over the requisite service period for awards expected to vest. The fair value of restricted stock and restricted stock units is determined based on the number of shares granted and the quoted price of our common stock on the date of grant. The determination of grant-date fair value for stock option awards is estimated using an option-pricing model, which includes variables such as the expected volatility of our share price, the anticipated exercise behavior of our employees, interest rates, and dividend yields. These variables are projected based on our historical data, experience, and other factors. Changes in any of these variables could result in material adjustments to the expense recognized for share-based payments.

Such value is recognized as an expense over the requisite service period, net of estimated forfeitures, using the straight-line attribution method. The estimation of stock awards that will ultimately vest requires judgment, and to the extent actual results or updated estimates differ from our current estimates, such amounts will be recorded as a cumulative adjustment in the period estimates are revised. We consider many factors when estimating expected forfeitures, including types of awards, employee class, and historical experience. Actual results and future estimates may differ substantially from our current estimates.

Warrants liability

February 2007 Financing

EITF 00-19 requires freestanding contracts that are settled in our own stock, including common stock warrants to be designated as an equity instrument, asset or liability. Under the provisions of EITF 00-19, a contract designated as an asset or a liability must be carried at fair value until exercised or expired, with any changes in fair value recorded in the results of operations. A contract designated as an equity instrument must be included within equity, and no subsequent fair value adjustments are required. We review the classification of the contracts at each balance sheet date. Pursuant to EITF 00-19, since we are unable to control all the events or actions necessary to settle the warrants in registered shares the warrants have been recorded as a current liability at fair value. The fair value of the outstanding warrants is evaluated at each reporting period with any resulting change in the fair value being reflected in the consolidated statements of operations. The change in fair value recognized in the financial statements during the years ended December 31, 2007 and December 31, 2008 was approximately $3.2 million and $3.5 million, respectively, with regards registered direct offering completed in February 2007. Fair value is estimated using an option-pricing model, which includes variables such as the expected volatility of our share price, interest rates, and dividend yields. These variables are projected based on our historical data, experience, and other factors. Changes in any of these variables could result in material adjustments to the expense recognized for changes in the valuation of the warrants liability.

Goodwill and Intangible Assets

Goodwill represents the difference between the purchase price and the fair value of net tangible and identifiable intangible assets acquired in the business combination. We recorded goodwill in March 2006 with respect to the merger with Xcyte and in October 2007 with respect to the acquisition of ALIGN. In accordance with FAS 142, we are required to test for impairment of goodwill, and intangible assets with indefinite lives which are not amortized, on an annual basis and at any other time if events occur or circumstances indicate that the carrying amount of goodwill and intangible assets may not be recoverable. Circumstances that could indicate impairment

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and require us to perform impairment tests more frequently than annually include significant adverse changes in market and economic conditions; adverse regulatory action; unanticipated competition or significant adverse change in perceived revenue potential.

We are organized as a single operating segment with two reporting units; ALIGN and Xcyte, to which goodwill was assigned along with relevant identifiable assets and liabilities. To test for impairment, we compared the fair value of each reporting unit to their respective carrying values, including assigned goodwill. To the extent the carrying amount of the reporting units exceeds its fair value; we compare the implied fair value of the reporting unit s goodwill with its carrying amount. The implied fair value of goodwill is determined by allocating the fair value of the reporting unit to all of the assets (recognized and unrecognized) and liabilities of the reporting unit in a manner similar to a purchase price allocation, in accordance with FAS No. 141 *Business Combinations*. The residual fair value after this allocation represents the implied fair value of the goodwill. To the extent the implied fair value of goodwill is less than its carrying amount we are required to recognize an impairment loss.

The fair value of our Xcyte reporting unit is determined by the market value of our outstanding common stock. However, the fair value of our ALIGN reporting unit is determined by using the income based valuation approach with respect to projected product sales. The income-based valuation measures the current value of the reporting unit by calculating the present value of its future cash flows using appropriate discount factors with regard to cost of capital experienced by entities of the same size and condition as us.

In September 2008, the goodwill acquired in the Xcyte transaction was written down in full and we recorded an impairment charge of approximately $2.7 million in accordance with FAS 142. This impairment charge was identified through our annual impairment review process and was triggered primarily by a decline in our stock price that reduced our market capitalization below book value of the net assets of the Xcyte reporting unit. Our reduced market capitalization reflected the general decline in the economic environment.

In December 2008, goodwill allocated to our ALIGN reporting unit following the ALIGN acquisition was fully written down in accordance with FAS 142, resulting in an impairment charge of approximately $1.6 million being recognized on the consolidated statement of operations. In determining the impairment charge, we considered the negative impact the current economic situation might have on sales growth expectations of the ALIGN products resulting in a downward revision of projected net cash flows from product sales. These factors caused the discounted cash flows for the reporting unit to be less than its carrying value on December 31, 2008.

Impairment of Long-Lived Assets

In accordance with FAS 144, when indicators of impairment exist, we assess the recoverability of the potentially affected long-lived assets by determining whether the carrying value of such assets can be recovered through undiscounted future operating cash flows. If impairment is indicated, we measure the amount of such impairment by comparing the carrying value of the asset to the estimated fair value of the related asset, which is generally determined based on the present value of the expected future cash flows.

Measurement of fair value is determined using the income-based valuation methodology. The income based valuation approach measures the current value of an asset (or asset group) by calculating the present value of the future expected cash flows to be derived from that asset, from the perspective of a market participant. Such cash flows are discounted using a rate of return that incorporates the risk-free rate for the use of funds, the expected rate of inflation and risks associated with using the asset. If the carrying amount of a long-lived asset exceeds its fair value, an impairment loss is recognized immediately and cannot be relieved at a later date.

Intangible assets acquired in the ALIGN transaction were also fully written down in September 2008, in accordance with FAS 144. An impairment charge of approximately $3.6 million was identified through our annual impairment review process and was recognized in the consolidated statement of operations. This one-time, non-cash charge was triggered by a downwards revision of projected net cash flows from product sales, required due to budgetary constraints experienced by health care providers and restrictions of the cost reimbursement regime. As a result the sum of the expected undiscounted cash flows was less than the carrying amount of the intangible assets on September 30, 2008.

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Recent Accounting Pronouncements

For information about recently issued accounting pronouncements please see Note 2 Summary of Significant Accounting Policies contained within notes to the consolidated financial statements.

In September 2006, the FASB issued FAS No. 157, *Fair Value Measurements,* (FAS 157), which establishes a framework for measuring fair value, and expands disclosures about fair value measurements. In February 2008, FASB issued FASB Staff Position Nos FAS 157-1, *Application of FASB Statement No. 157 to FASB Statement No. 13 and Other Accounting Pronouncements That Address Fair Value Measurements for Purposes of Lease Classification or Measurement under Statement 13* (FSP FAS 157-1) and FAS 157-2, *Effective Date of FASB Statement No. 157* (FSP FAS 157-2). FSP FAS 157-1 amends FAS 157 to remove certain leasing transactions from its scope. FSP FAS 157-2 delays the effective date of FAS 157 for all non-financial assets and non-financial liabilities, except for items that are recognized or disclosed at fair value in the financial statements on a recurring basis. FAS 157 is effective for the Company beginning January 1, 2009 for these items. The effective date for financial assets and liabilities and non-financial items that are recognized on a recurring basis was January 1, 2008. The partial adoption of FAS 157 by the Company in 2008 has not had a material effect on the Company s consolidated financial statements, and the remaining adoption in 2009 is not expected to have a material effect on the Company s consolidated financial statements based on our current and forecasted business activities

In February 2007, the FASB issued FAS No. 159, *The Fair Value Option for Financial Assets and Financial Liabilities* (FAS 159) which permits entities to choose to measure many financial instruments and certain other items at fair value that are not currently required to be measured at fair value. FAS 159 was effective for the Company on January 1, 2008 and the adoption of FAS 159 did not have a material impact on our consolidated financial statements.

In June 2007, FASB ratified the consensus reached by the EITF on EITF Issue No. 07-3, *Accounting for Nonrefundable Advance Payments for Goods or Services to Be Used in Future Research and Development Activities* (EITF 07-3). EITF 07-3 addresses the diversity that exists with respect to the accounting for the non-refundable portion of a payment made by a research and development entity for future research and development activities. Under EITF 07-3, an entity would defer and capitalize non-refundable advance payments made for research and development activities until the related goods are delivered or the related services are performed. EITF 07-3 was effective for new contracts entered into by the Company from January 1, 2008. The adoption of EITF 07-3 has not had a material effect on our consolidated financial statements.

In October 2008, FASB issued FASB Staff Position No. FAS 157-3, *Determining the Fair Value of a Financial Asset When the Market for that Asset Is Not Active* (FSP FAS 157-3), which clarifies the application of FAS 157 as it relates to the valuation of financial assets in a market that is not active for those financial assets. FSP FAS 157-3 was effective immediately, including those periods for which financial statements had not been issued and was adopted by the Company, as it applies to its financial instruments effective January 1, 2008. The adoption of FSP FAS 157-3 has not had a material impact on our consolidated financial statements.

In November 2007, the FASB issued FAS No. 141 (revised 2007), *Business Combinations* (FAS 141(R)) and FAS No. 160, *Noncontrolling Interests in Consolidated Financial Statements, an amendment of ARB No. 51* (FAS 160). FAS 141(R) will change how business acquisitions are accounted for and will impact financial statements both on the acquisition date and in subsequent periods. FAS 160 will change the accounting and reporting for minority interests, which will be recharacterized as noncontrolling interests and classified as a component of equity. FAS 141(R) and FAS 160 are effective the Company beginning January 1, 2009. FAS 141(R) will be applied prospectively. FAS 160 requires retroactive adoption of the presentation and disclosure requirements for existing minority interests. All other requirements of FAS 160 will be applied prospectively. Early adoption is prohibited for both standards. The adoption of FAS 141(R) and FAS 160 is not expected to have a material impact on the Company s

consolidated financial statements.

In December 2007, FASB ratified the consensus reached by Emerging Issues Task Force (EITF) on EITF Issue 07-1, Accounting for Collaborative Arrangements (EITF 07-1). EITF 07-1 requires collaborators to present the results of activities for which they act as the principal on a gross basis and report any payments received from (made to) other collaborators based on other applicable Generally Accepted Accounting Principles (GAAP)

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or, in the absence of other applicable GAAP, based on analogy to authoritative accounting literature or a reasonable, rational, and consistently applied accounting policy election. Further, EITF 07-1 clarified that the determination of whether transactions within a collaborative arrangement are part of a vendor-customer (or analogous) relationship subject to EITF 01-9, Accounting for Consideration Given by a Vendor to a Customer (Including a Reseller of the Vendor s Products) . EITF 07-1 will be effective for the Company beginning January 1, 2009 and will be applied retrospectively to all prior periods presented for all collaborative arrangements existing as of the effective date. The adoption of EITF 07-1 is not expected to have a material effect on the Company s consolidated financial statements based on our current and forecasted business activities.

In May 2008, the FASB issued FASB Staff Position APB 14-1 Accounting for Convertible Debt Instruments That May Be Settled in Cash upon Conversion (Including Partial Cash Settlement) (FSP APB 14-1). FSP APB 14-1 requires the issuer of certain convertible debt instruments that may be settled in cash (or other assets) on conversion to separately account for the liability (debt) and equity (conversion option) components of the instrument in a manner that reflects the issuer s non-convertible debt borrowing rate. FSP APB 14-1 is effective for fiscal years beginning after December 15, 2008 on a retroactive basis and will be adopted by the Company in the period beginning January 1, 2009. The adoption of FSP APB 14-1 is not expected to have a material impact on the Company s consolidated financial statements.

In June 2008, FASB ratified the consensus reached by the EITF on EITF Issue No. 07-5, *Determining Whether an Instrument (or Embedded Feature) Is Indexed to an Entity s Own Stoc*k (EITF 07-5). EITF 07-5 provides guidance for determining whether an equity-linked financial instrument, or embedded feature, is indexed to an entity s own stock. EITF 07-5 is effective for the Company beginning January 1, 2009. The Company does not expect the adoption of EITF 07-5 to have a material impact on its consolidated financial statements.

Item 7A. ***Quantitative and Qualitative Disclosures About Market Risk***

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

Investment and Interest Rate Risk

Financial instruments which potentially subject us to interest rate risk consist principally of cash and cash equivalents and short-term investments. At December 31, 2008, our cash and cash equivalents of $25.7 million are primarily invested in highly liquid money market accounts, Federal agency obligations & municipal bonds and commercial paper; and our short-term investments consisted of $1.5 million in corporate bonds with remaining maturities of one year or less.

The primary objective of our investment activities is to preserve principal while at the same time maximizing yields without significantly increasing risk. Pursuant to our investment guidelines, all investments in commercial paper & corporate bonds of financial institutions and corporations are rated A or better by both Moody s and Standard and Poor s, no one individual security shall have a maturity of greater than 18 months and investments in any one corporation is restricted to 5% of the total portfolio. To minimize our exposure to adverse shifts in interest rates, we invest in short-term instruments and at December 31, 2008 we held no investments with a maturity in excess of one year. Due to the short-term nature of our investments, portfolio diversification, and our investment policy we believe that our exposure to market interest rate fluctuations is minimal, liquidity is maintained and we do not have a material financial market risk exposure.

A hypothetical 10% change in short-term interest rates from those in effect at December 31, 2008 would not have a significant impact on our financial position or our expected results of operations, however we may continue to have

risk exposure to our holdings in cash, money market accounts and cash equivalents, which may adversely impact the fair value of our holdings. As of December 31, 2008, there were no indicators of credit risk impact to the valuation of our cash, cash equivalents or short term investments. We do not currently hold any derivative financial instruments with interest rate risk.

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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. Intercompany loans with this subsidiary are denominated in U.S. dollars and unrealized foreign exchange gains and losses arising on these loans have been recorded in the consolidated statement of operations within the separate line item foreign exchange gains/(losses) within other income (expense) up to September 30, 2008.

During the year ended December 31, 2008 there were unfavorable unrealized foreign exchange movements of approximately $17.2 million on intercompany loans due to the increase in the strength of the United States dollar against the British pound. Of this $4.8 million is recorded in the consolidated statement of operations within the separate line item foreign exchange gains/(losses), within other income (expense). This has been offset by a realized gain of $0.3 million on transactions in the year in respect of underlying operations, resulting in a net foreign exchange loss of $4.5 million.

In conjunction with the operational review conducted by us in September 2008, the nature of intercompany funding was considered. It was concluded that as repayment of intercompany loans is not expected in the foreseeable future, the nature of the funding advanced was of a long-term investment nature and that the terms of the loans should be amended to reflect this. Effective October 1, 2008, intercompany loans ceased to be repayable on demand and have no fixed repayment date. As a result of the change in repayment terms, from October 1, 2008 all unrealized foreign exchange gains or losses arising on intercompany loans is recognized in other comprehensive income. This has restricted the unfavorable unrealized foreign exchange movements recorded in other income to $4.8 million, with $12.3 million recognized in other comprehensive income for the three months from October 1, 2008 to December 31, 2008. Future unrealized foreign exchange gains or losses arising on the intercompany loans will be recognized in other comprehensive income on the consolidated statement of stockholders equity until repayment of the intercompany loan becomes foreseeable.

We currently do not engage in foreign currency hedging. We enter into certain transactions denominated in foreign currencies in respect of underlying operations and, therefore, we are subject to currency exchange risks. During the year ended December 31, 2008, we realized gains of approximately $0.3 million on such transactions. Other differences on foreign currency translation arising on consolidation of $14.9 million are also recorded as a movement in other comprehensive income.

Common Stock Price Risk

In February 2007, we issued common stock and warrants. Pursuant to EITF 00-19, we recorded the fair value of the warrants as a current liability. The fair value of the outstanding warrants is evaluated at each reporting period with any resulting change in the fair value being reflected in the condensed consolidated statements of operations. The change in fair value recognized in the financial statements during the years to December 31, 2007 and 2008 was $3.2 million and $3.5 million, respectively. Fair value of the derivative instruments will be affected by estimates of various factors that may affect the respective instrument, including our stock price, the risk free rate of return and expected volatility in the fair value of our stock price. 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.

In December 2007, we entered into a CEFF with Kingsbridge, in which Kingsbridge committed to provide us up to $60 million of capital during the next three years. We may access capital under the CEFF in tranches, with each tranche being issued and priced over an eight-day pricing period. Kingsbridge will purchase shares of common stock

pursuant to the CEFF at discounts ranging from 6% to 10% depending on the average market price of the common stock during the eight-day pricing period, provided that the minimum acceptable purchase price for any shares to be issued to Kingsbridge during the eight-day period is determined by the higher of $2.50 or 90% of our common stock closing price the day before the commencement of each draw down.

As of December 31, 2008, we have not drawn down any funds under the CEFF. Since June 16, 2008, we were unable to draw down any amounts under the CEFF as the closing price of our common stock did not exceed $2.50 per share.

Item 8. ***Financial Statements and Supplementary Data***

INDEX TO CYCLACEL PHARMACEUTICALS, INC. FINANCIAL STATEMENTS

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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, 2008 and 2007, and the related consolidated statements of operations, stockholders equity, and cash flows for each of the three years in the period ended December 31, 2008 and the period from August 13, 1996 (inception) to December 31, 2008. 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, 2008 and 2007, and the consolidated results of its operations and its consolidated cash flows for each of the three years in the period ended December 31, 2008 and for the period from August 13, 1996 (inception) to December 31, 2008, in conformity with U.S. generally accepted accounting principles.

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, 2008, 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 31, 2009 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

London, England
March 31, 2009

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CYCLACEL PHARMACEUTICALS, INC.
(A Development Stage Company)

CONSOLIDATED BALANCE SHEETS

	December 31,	
	2007	2008
	(In $000s, except share amounts)	
ASSETS		
Current assets:		
Cash and cash equivalents	30,987	24,220
Short-term investments	27,766	1,502
Inventory	213	508
Prepaid expenses and other current assets	4,811	2,784
Total current assets	63,777	29,014
Property, plant and equipment (net)	3,016	1,748
Deposits and other assets	196	195
Intangible assets (net)	4,305	
Goodwill	4,618	
Total assets	75,912	30,957
LIABILITIES AND STOCKHOLDERS EQUITY		
Current liabilities:		
Accounts payable	4,958	754
Accrued liabilities	3,979	5,186
Other current liabilities	1,315	1,615
Warrants liability	3,545	43
Current portion of other accrued restructuring charges	905	1,029
Current portion of equipment financing	10	
Total current liabilities	14,712	8,627
Other accrued restructuring charges, net of current	2,090	1,062
Other long term payables	1,141	626
Total liabilities	17,943	10,315
Commitments and contingencies (Note 12)		
Stockholders equity:		
Preferred stock, $0.001 par value; 5,000,000 shares authorized at December 31, 2007 and 2008, respectively; 2,046,813 shares issued and outstanding at December 31, 2007 and 2008, respectively. Aggregate preference in liquidation of $20,673,000 at December 31, 2007 and December 31, 2008	2	2
	20	20

Common stock, $0.001 par value; 100,000,000 shares authorized at December 31, 2007 and 2008, respectively; 20,433,129 shares issued and outstanding at December 31, 2007 and 2008, respectively		
Additional paid-in capital	222,906	223,377
Accumulated other comprehensive loss	(2,630)	(42)
Deficit accumulated during the development stage	(162,329)	(202,715)
Total stockholders equity	57,969	20,642
Total liabilities and stockholders equity	75,912	30,957

The accompanying notes are an integral part of these consolidated financial statements.

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CYCLACEL PHARMACEUTICALS, INC.
(A Development Stage Company)

CONSOLIDATED STATEMENTS OF OPERATIONS

	Year Ended December 31, 2006	Year Ended December 31, 2007	Year Ended December 31, 2008	Period from August 13, 1996 (Inception) to December 31, 2008
	(In $000s, except share and per share amounts)			
Revenues:				
Collaboration and research and development revenue	231	10		3,000
Product Revenue			838	838
Grant revenue	156	119	39	3,635
	387	129	877	7,473
Operating expenses:				
Cost of goods sold			429	429
Research and development	21,205	19,569	18,869	160,413
Selling, general and administrative	12,598	12,033	15,354	63,308
Goodwill and intangibles impairment			7,934	7,934
Other restructuring costs	225	1,554	489	2,268
Total operating expenses	34,028	33,156	43,075	234,352
Operating loss	(33,641)	(33,027)	(42,198)	(226,879)
Other income (expense):				
Costs associated with aborted 2004 IPO				(3,550)
Change in valuation of derivative	(215)	(93)		(308)
Change in valuation of warrants liability		3,205	3,502	6,707
Foreign exchange gains / (losses)	279	490	(4,501)	(4,043)
Interest income	2,328	3,554	1,380	13,541
Interest expense	(254)	(223)	(318)	(4,457)
Total other income, net	2,138	6,933	63	7,890
Loss before taxes	(31,503)	(26,094)	(42,135)	(218,989)
Income tax benefit	2,245	2,041	1,749	16,274
Net loss	(29,258)	(24,053)	(40,386)	(202,715)
Dividends on Preferred Ordinary shares	(2,827)			(38,123)
	(32,085)	(24,053)	(40,386)	(240,838)

Net loss applicable to common shareholders				
Net loss per share	basic and diluted	$ (2.40)	$ (1.21)	$ (1.98)
Weighted average common shares outstanding		13,390,933	19,873,911	20,433,129

The accompanying notes are an integral part of these consolidated financial statements.

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CYCLACEL PHARMACEUTICALS, INC.
(A Development Stage Company)

CONSOLIDATED STATEMENTS OF STOCKHOLDERS EQUITY (DEFICIT)

	Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Income/(Loss)	Deferred Compensation	Deficit Accumulated During Development Stage	Total
	No.	$000	No.	$000	$000	$000	$000	$000	$000
	(In $000s, except share and per share amounts)								
On incorporation, Issue of shares for cash					1				1
Translation adjustment						(4)			(4)
Loss for the period								(290)	(290)
Comprehensive loss for the period									(294)
Balance at March 31, 1997					1	(4)		(290)	(293)
Issue of shares for cash, net of issuance costs			266,778		4,217				4,217
Issue of shares for IP rights agreement					262				262
Deferred stock-based compensation					2,002		(2,002)		
Amortization of deferred stock-based compensation							302		302
Translation adjustment						55			55
Loss for the year								(2,534)	(2,534)
Comprehensive loss for the year									(2,479)
Balance at March 31, 1998			266,778		6,482	51	(1,700)	(2,824)	2,009
Amortization of deferred stock-based compensation							406		406
Translation adjustment						11			11
Loss for the year								(3,964)	(3,964)
Comprehensive loss for the year									(3,953)

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CYCLACEL PHARMACEUTICALS, INC.
(A Development Stage Company)

CONSOLIDATED STATEMENTS OF STOCKHOLDERS EQUITY (DEFICIT) (Continued)

	Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income/(Loss)	Deferred Compensation	Deficit Accumulated During Development Stage	Total
	No.	$000	No.	$000	$000	$000	$000	$000	$000
	(In $000s, except share and per share amounts)								
Balance at March 31, 1999			266,778		6,482	62	(1,294)	(6,788)	(1,538)
Issue of shares for cash, net of issuance costs			538,889	1	12,716				12,717
Issue of shares on conversion of bridging loan			90,602		1,638				1,638
Issue of shares in lieu of cash bonus			9,060		164				164
Issue of shares for research & development agreement					409				409
Exercise of share options			2,265		40				40
Deferred stock-based compensation					167		(167)		
Amortization of deferred stock-based compensation							433		433
Translation adjustment						(194)			(194)
Loss for the year								(5,686)	(5,686)
Comprehensive loss for the year									(5,880)
Balance at March 31, 2000			907,594	1	21,616	(132)	(1,028)	(12,474)	7,983
Deferred stock-based compensation					294		(294)		
Amortization of deferred stock-based compensation							275		275
Translation adjustment						(466)			(466)

Loss for the year						(10,382)	(10,382)
Comprehensive loss for the year							(10,848)
Balance at March 31, 2001	907,594	1	21,910	(598)	(1,047)	(22,856)	(2,590)
Issue of shares for cash, net of issuance costs	5,451						
Exercise of share options for cash			106				106
Issue of shares for license agreement	4,510		183				183
Fair value of warrants issued to shareholders			1,215				1,215
Deferred stock-based compensation			363		(363)		
Amortization of deferred stock-based compensation					672		672