Cyclacel Pharmaceuticals, Inc.
Form POS AM
May 27, 2011

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As filed with the Securities and Exchange Commission on May 27, 2011
Registration No. 333-167470

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

POST-EFFECTIVE AMENDMENT NO. 2 TO FORM S-1 ON FORM S-3

REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933

CYCLACEL PHARMACEUTICALS, INC.
(Exact name of registrant as specified in its charter)

Delaware	**91-1707622**
(State or other jurisdiction of incorporation or organization)	(IRS Employer Identification Number)

200 Connell Drive, Suite 1500
Berkeley Heights, NJ 07922
(908) 517-7330
(Address, including zip code, and telephone number, including area code, of registrant s principal executive offices)

Spiro Rombotis
President and Chief Executive Officer
Cyclacel Pharmaceuticals, Inc.
200 Connell Drive, Suite 1500
Berkeley Heights, NJ 07922
(908) 517-7330
(Name, address, including zip code, and telephone number, including area code, of agent for service)

With a copy to:

Joel I. Papernik, Esq.
Jeffrey P. Schultz, Esq.
Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.
666 Third Avenue
New York, New York 10017
(212) 935-3000

Approximate date of commencement of proposed sale to the public: From time to time after this Registration Statement becomes effective.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box. o

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box. þ

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement

for the same offering. o

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box. o

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box. 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. o

Large accelerated filer	Accelerated filer	Non-accelerated filer	Smaller reporting company
o	o	o	þ

(Do not check if a smaller reporting company)

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until the registration statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

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Explanatory Note

On December 11, 2007, the registrant filed a registration statement with the Securities and Exchange Commission (the Commission) on Form S-3 (Registration No. 333-167470), which was declared effective by the Commission on December 20, 2007 (as amended, the Form S-3), to register for disposition by the selling stockholder named in this Prospectus up to 100,000 shares of the registrant s common stock, $0.001 par value.

On May 16, 2011, the registrant filed a Post-Effective Amendment No. 1 on Form S-1 to Form S-3 to convert such registration statement on Form S-3 into a registration statement on Form S-1. This Post-Effective Amendment No. 2 to Form S-1 on Form S-3 is being filed by the registrant to convert the Form S-1 into a registration statement on Form S-3, and contains an updated prospectus relating to the offering and sale of the shares that were registered for resale on the Form S-3.

All filing fees payable in connection with the registration of these securities were previously paid by the registrant in connection with the filing of the original registration statement.

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The information in this Prospectus is not complete and may be changed. The selling stockholder may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This Prospectus is not an offer to sell these securities and is not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to Completion, dated May 27, 2011

PROSPECTUS

100,000 Shares of Common Stock
CYCLACEL PHARMACEUTICALS, INC.
Common Stock, $0.001 Par Value

This Prospectus relates to the disposition from time to time of up to 100,000 shares of common stock, par value $0.001 per share, by the selling stockholder identified herein. The shares of common stock registered for resale under this prospectus are up to 100,000 shares of our common stock that we may issue upon exercise of an amended and restated warrant we issued to the Selling Stockholder, Kingsbridge Capital Limited, or Kingbridge, on November 24, 2009.

The shares may be sold or otherwise disposed of from time to time by the selling stockholder. All expenses of the registration incurred in connection herewith are being borne by us, but any brokers fees or commissions will be borne by the selling stockholder. We may receive proceeds upon the issuance of shares to Kingsbridge or in connection with the exercise of the warrant by Kingsbridge.

Our common stock is listed on the NASDAQ Global Market under the symbol CYCC. On May 25, 2011, the last reported sale price for our common stock was $1.57 per share.

Investing in our securities involves significant risks. We strongly recommend that you read carefully the risks we describe in this Prospectus and the risk factors that are incorporated by reference in this Prospectus from our filings made with the Securities and Exchange Commission. See Risk Factors beginning on page 9 before deciding whether to invest in our common stock.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the accuracy or adequacy of this Prospectus. Any representation to the contrary is a criminal offense.

The date of this Prospectus is _____, 2011.

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You should read this Prospectus and the documents incorporated by reference carefully before you invest. Such documents contain important information you should consider when making your investment decision. See Incorporation of Documents by Reference on page 42. You should rely only on the information provided in this Prospectus or documents incorporated by reference in this Prospectus. We have not authorized anyone to provide you with different information. The information contained in this Prospectus is accurate only as of the date of this Prospectus and any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this Prospectus or of any sale of our common stock. Our business, financial condition, results of operations and prospects may have changed since that date.

Persons outside the United States who come into possession of this Prospectus must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock and the distribution of this Prospectus outside of the United States.

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PROSPECTUS SUMMARY

Because this is only a summary, it does not contain all of the information that may be important to you. You should carefully read the more detailed information contained in this Prospectus and the information incorporated by reference carefully before you invest. Our business involves significant risks. You should carefully consider the information under the heading Risk Factors beginning on page 9.

As used in this Prospectus, unless otherwise indicated, the terms we, us, our company, the Company and Cyclacel refer to Cyclacel Pharmaceuticals, Inc., a Delaware corporation.

Our Business

We are a biopharmaceutical company dedicated to the development and commercialization of novel, mechanism-targeted drugs to treat human cancers and other serious diseases. We are focused on delivering leading edge therapeutic management of cancer patients based on a clinical development pipeline of novel drug candidates.

Clinical programs

Our clinical development priorities are focused on orally-available sapacitabine in the following indications:

- AML in the elderly;
- Myelodysplastic syndromes, or MDS; and
- Non-small cell lung cancer, or NSCLC.

We have a Special Protocol Assessment, or SPA, agreement with the U.S. Food and Drug Administration, or FDA, on the design of a pivotal Phase 3 trial for our sapacitabine oral capsules, the SEAMLESS trial, as a front-line treatment in elderly patients aged 70 years or older with newly diagnosed AML who are not candidates for intensive induction chemotherapy. SEAMLESS is a registration-directed, clinical trial of sapacitabine oral capsules to be conducted under the SPA and will be a randomized study against an active control drug with the primary objective of demonstrating an improvement in overall survival.

We have additional ongoing programs in clinical development which are currently pending the availability of clinical data. Once these data become available and are reviewed, we will determine the feasibility of pursuing further development and/or partnering of these assets including sapacitabine in combination with seliciclib, seliciclib in nasopharyngeal cancer, or NPC, and NSCLC and CYC116.

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 agents by regulating 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.

Although our resources are primarily directed towards advancing our anticancer drug candidate sapacitabine through in-house development activities we are also progressing, but with lower levels of investment than in previous years, our other 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.

Sapacitabine

Our lead 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 and repair 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, and 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 and 5-FU, two widely used nucleoside analogs, in delaying the onset and growth of liver metastasis. We have retained worldwide rights to commercialize sapacitabine, except for Japan, for which Daiichi-Sankyo Co., Ltd.,

or Daiichi-Sankyo, has a right of first negotiation.

We are currently exploring sapacitabine in both hematological cancers and solid tumors. To date, sapacitabine has been evaluated in approximately 400 patients in several Phase 1 and 2 studies and has shown signs of anti-cancer activity. In January 2011, we opened enrollment of the SEAMLESS pivotal Phase 3 trial, which will evaluate sapacitabine oral capsules as a front-line treatment in elderly patients aged 70 years or older with newly-diagnosed AML who are not candidates for intensive induction chemotherapy. The study will be conducted under an SPA.

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Hematological Cancers

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

In December 2007, at the ASH annual meeting, we reported interim results from a Phase 1 clinical trial of oral sapacitabine in patients with advanced leukemias and MDS. The data 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 conducted at The University of Texas M. D. Anderson Cancer Center and is led by Hagop Kantarjian, M.D., 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.

Phase 2 randomized clinical trial in elderly patients with AML previously untreated or in first relapse

In December 2007, we initiated an open-label, multicenter, randomized Phase 2 clinical trial of oral sapacitabine in 60 elderly patients with AML aged 70 or older who are previously untreated or in first relapse. The Phase 2 study, led by Dr. Kantarjian, has a primary endpoint of 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 CR or CRp, partial remission, or PR, duration of CR or CRp, or major 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 arms, A. 200 mg twice daily for seven days every 3-4 weeks, B. 300 mg twice daily for seven days every 3-4 weeks, and C. 400 mg twice daily for three days per week for two weeks every 3-4 weeks, which produces a better 1-year survival rate in the event that all three dosing schedules are active. Each arm enrolled and treated 20 patients. Approximately 55% of patients had AML de novo and the rest had AML preceded by antecedent hematological disorder, or AHD, such as MDS, or myeloproliferative disease. Eighty percent of the patients were untreated and 20% in first relapse. We completed enrollment of 60 AML patients in this study in October 2008. In December 2009, at the 51st Annual Meeting of ASH we reported 1-year survival data.

The primary endpoint of 1-year survival was 35% on Arm A, 30% on Arm C and 10% on Arm B. The median overall survival was 212 days on Arm C (range of 13 to over 654 days), 197 days on Arm A (range of 26 to over 610 days) and 100 days on Arm B (range of 6 to over 646 days). Overall response rate, or ORR, a secondary endpoint, was 45% on Arm A, 35% on Arm C and 25% on Arm B with CR rate of 25% on Arm C and 10% on Arms A and B. Thirty-day mortality was 10% on Arm C and Arm A and 20% on Arm B. Approximately 30% of all patients received sapacitabine for at least 6 cycles. Fifteen patients who survived one year or more received an average of 12 treatment cycles.

Exploratory subgroup analysis suggests that (i) Arm C may be more effective for de novo AML and (ii) Arm A may be more effective for AML preceded by AHD, such as MDS.

The 3-day dosing schedule in Arm C was selected for further clinical development in elderly patients with de novo AML based on a 1-year survival rate of 30%, ORR of 35% with durable CRs. The 7-day dosing schedule in Arm A was selected for further clinical development in elderly patients with AML preceded by AHD based on a 1-year survival rate of 35%, ORR of 45% with durable hematological improvement.

Randomized Phase 2 clinical trial in older patients with MDS as a second-line treatment

In September 2008, we advanced sapacitabine into Phase 2 development as a second-line treatment in patients aged 60 or older with MDS who are previously treated with hypomethylating agents. The MDS stratum of the study is designed as a protocol amendment expanding the ongoing Phase 2 trial of sapacitabine in AML described above, to include a cohort of patients with MDS. Patients with MDS often progress to AML. The primary objective of the MDS

stratum is to evaluate the 1-year survival rate of three dosing schedules of sapacitabine. Secondary objectives are to assess the number of patients who have achieved CR or CRp, PR, 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 1-year survival rate for each stratum in the event that all three dosing schedules are active.

In December 2010, at the ASH annual meeting, we reported 1-year survival data from a Phase 2 randomized trial of oral sapacitabine capsules, a novel nucleoside analogue, in older patients with MDS refractory to hypomethylating agents, such as azacitidine and decitabine.

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The study uses a selection design with the objective of identifying a dosing schedule that produces a better 1-year survival rate in the event that all three dosing schedules are active. The study enrolled 61 patients aged 60 or older with MDS refractory to hypomethylating agents randomized across three dosing schedules of sapacitabine: 21 patients in Arm A, a 7-day low dose regimen (200 mg b.i.d.); 20 patients in Arm B, a 7-day high dose regimen (300 mg b.i.d.) and 20 patients in Arm C, a 3-day high dose regimen (400 mg b.i.d.). Approximately 77% of patients were aged 70 years or older and 84% were scored as intermediate-2 or high risk by IPSS, the International Prognostic Scoring System. Baseline blast counts were between 11% and 29% in 51% of the patients. All patients were previously treated with hypomethylating agents: 43% with azacitidine, 34% with decitabine and 23% were double refractory patients as they were treated with both azacitidine and decitabine (7 on Arm A, 4 on Arm B and 3 on Arm C). Approximately 16% were previously treated with lenalidomide in addition to hypomethylating agents.

The primary endpoint of 1-year survival was achieved in 29% of the patients on Arm A, 30% of the patients on Arm B and 35% of the patients on Arm C. The median overall survival was 217 days on Arm A (range of 15 to 663 days), 232 days on Arm B (range of 37 to over 811 days) and 236 days on Arm C (range of 16 to over 672 days). Overall response rate, a secondary endpoint consisting of the rate of CR, CRp, PR, CRi or hematological improvement, was 24% for patients on Arm A, 35% for patients on Arm B and 15% for patients on Arm C. Two patients achieved a CR both on Arm A. Approximately 20% of all patients received sapacitabine for 4 to 6 cycles and 15% for 7 or more cycles. The mortality rate from all causes within thirty days of randomization was 6.6%.

Randomized Phase 3 pivotal trial, SEAMLESS, as a front-line treatment in elderly patients aged 70 years or older with newly diagnosed AML who are not candidates for intensive induction chemotherapy

On January 11, 2011, we opened enrollment of the SEAMLESS pivotal Phase 3 trial for the Company s sapacitabine oral capsules as a front-line treatment of elderly patients aged 70 years or older with newly diagnosed AML who are not candidates for intensive induction chemotherapy. The study is being conducted under an SPA agreement that Cyclacel reached with the FDA. SEAMLESS builds on promising 1-year survival observed in elderly patients aged 70 years or older with newly diagnosed AML or AML in first relapse enrolled in a Phase 2 study of single agent sapacitabine.

The SEAMLESS study is chaired by Hagop M. Kantarjian, M.D., Chairman and Professor, Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, Texas. SEAMLESS is a multicenter, randomized, Phase 3 study comparing three treatment arms. In Arm A sapacitabine is administered in alternating cycles with decitabine, in Arm B sapacitabine is administered alone and in Arm C decitabine is administered alone. The primary efficacy endpoint is overall survival. The study is designed to demonstrate an improvement in overall survival of either of two pairwise comparisons: (1) Arm A versus Arm C or (2) Arm B versus Arm C. Approximately 150 patients per arm or a total of 450 patients from approximately 50 centers will be enrolled. SEAMLESS will be monitored by a Data Safety Monitoring Board (DSMB). A prespecified interim analysis for futility will be performed and reviewed by the DSMB.

On September 13, 2010, we reached agreement with the FDA regarding the SPA, on the design of a pivotal Phase 3 trial, the SEAMLESS trial. An SPA provides trial sponsors with an FDA agreement that the design and analysis of the trial adequately address objectives in support of a submission for a marketing application if the trial is performed according to the SPA. The SPA may only be changed through a written agreement between the sponsor and the FDA, or if the FDA becomes aware of a substantial scientific issue essential to product efficacy or safety. However, an SPA does not provide any assurance that a marketing application would be approved by the FDA. Furthermore, Phase 3 clinical trials are time-consuming and expensive, and because we have limited resources, we may be required to collaborate with a third party or raise additional funds. However, there is no assurance that we will be able to do so.

Solid Tumors

Phase 1 clinical trials in patients with refractory solid tumors or lymphomas

Two Phase 1 studies of sapacitabine were completed by Daiichi-Sankyo, from which we in-licensed sapacitabine, evaluating 87 patients in refractory solid tumors. In addition, we conducted a Phase 1b dose escalation clinical trial in patients with refractory solid tumors or lymphomas. Preliminary results of the Phase 1b study were reported at the EORTC-NCI-AACR Molecular Targets and Cancer Therapeutics meeting 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 non-small cell lung cancer

In January 2009, we began 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., at 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, 1-year survival, overall survival and safety. The study will enroll approximately 40 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.

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Phase 2 clinical trial in patients with cutaneous T-cell lymphoma, or 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 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. Non-hematological toxicities were mostly mild to moderate. The best response by investigator assessment was partial response in 3 patients out of 16 enrolled. We stopped the trial in order to re-direct our resources to sapacitabine clinical trials with a higher priority.

Orphan Designation

European Union

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. 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.

United States

In June 2010, we announced that the FDA granted orphan drug designation to our sapacitabine product candidate for the treatment of both AML and MDS. An orphan designation in the United States confers a range of benefits to sponsor companies, including market exclusivity for a period of seven years from the date of drug approval, the opportunity to apply for grant funding from the United States government to defray costs of clinical trial expenses, tax credits for clinical research expenses and a potential waiver of the FDA s application user fee. Orphan status is granted by the FDA to promote the development of new drug therapies for the treatment of diseases that affect fewer than 200,000 individuals in the United States.

Seliciclib

Although our current clinical development priorities are focused on sapacitabine only, our second drug candidate, seliciclib, is a novel, first-in-class, orally-available, CDK inhibitor. The compound selectively inhibits a spectrum of enzyme targets -CDK2, CDK7 and CDK9- that are central to the process of cell division and cell cycle control. The target profile of seliciclib is differentiated from the published target profile of other CDK inhibitors. Its selectivity is differentiated by recent publications by independent investigators which showed that seliciclib (i) is more active against NSCLC cells with K-Ras or N-Ras mutations than those with wild type Ras and (ii) overcomes resistance to letrozole (Femara®) in breast cancer cells caused by a particular form of cyclin E in complex with CDK2. 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 450 patients in several Phase 1 and 2 studies and has shown signs of anti-cancer activity. We have retained worldwide rights to commercialize seliciclib.

Phase 1 clinical trials in patients with refractory solid tumors

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, measured as a decrease in the size of primary tumor and

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

Phase 2 clinical trials in patients with NSCLC or breast cancer

Four Phase 2 trials have been conducted in cancer patients to evaluate the tolerability and antitumor activities of seliciclib alone or in combination with standard chemotherapies used in the treatment of advanced NSCLC or breast cancer. Interim data from two Phase 2 open-label studies of a total of 52 patients with NSCLC, suggest that seliciclib treatment did not aggravate the known toxicities of standard first and second-line chemotherapies nor appear to cause unexpected toxicities, although these trials were not designed to provide statistically significant comparisons. The combination of seliciclib with a standard dose of capecitabine (Xeloda®) was not well tolerated in patients with advanced breast cancer.

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On December 21, 2010, we announced topline results from APPRAISE, our Phase 2b, randomized discontinuation, double-blinded, placebo-controlled, study of oral seliciclib capsules as a third line or later treatment in patients with NSCLC. Topline results, after unblinding the treatment assignment among randomized patients, showed that there was no difference between the seliciclib and placebo arms in terms of progression free survival, or PFS, (48 versus 53 days respectively) but an increase in median overall survival was observed favoring the seliciclib arm over the placebo arm (388 versus 218 days respectively). A total of 187 patients from 21 centers in the United States were entered in the study after having progressed on at least two prior therapeutic regimens for their NSCLC. Of these, 53 (28%) were randomized, 27 on seliciclib and 26 on placebo. Forty-five out of 53 randomized patients (85%) received 3 or more prior therapies and 45 out of 53 randomized patients (85%) previously received at least one EGFR inhibitor drug (22 on seliciclib and 23 on placebo). Fourteen patients were crossed-over to the seliciclib arm after their cancer progressed while they were receiving placebo. Study data demonstrated seliciclib to be safe at the administered dose. There was no difference between the seliciclib and placebo arms in terms of PFS of 48 days on the seliciclib arm versus 53 days on the placebo arm. However an increase in median overall survival was observed of 388 days on the seliciclib arm versus 218 days on the placebo arm.

APPRAISE was 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 was led by Chandra P. Belani, M.D. at Milton S. Hershey Medical Center, Penn State University. The study s main objective was to learn the anti-tumor activity of seliciclib as a single agent in refractory NSCLC and help determine further development strategies. The study design was randomized discontinuation. All patients received seliciclib at a dose of 1200 mg twice a day for three days for at least three cycles of two weeks each. Patients who achieved stable disease after three cycles were randomized to continue on seliciclib or receive placebo with best supportive care. Patients in the placebo arm who progressed were given the option to cross-over and again receive seliciclib. The primary efficacy endpoint of APPRAISE was doubling progression free survival, or PFS, measured in the randomized portion of the study.

In August 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 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 main conclusions: there were no safety concerns that would warrant stopping the study; there was no trend favoring the seliciclib treatment arm; and as a definitive conclusion could not be reached because of the low number of events, it was recommended that the study be continued. Based on our cost versus benefit analysis, we decided not to enroll additional patients. The APPRAISE trial continued with the 191 patients already enrolled until the last enrolled patient had completed follow-up. In accordance with the protocol, we remain blinded to the study data during the whole process.

Phase 2 clinical trials 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 dependent on clinical data from the lead-in phase and available resources.

In May 2009, at the ASCO annual meeting, we reported interim data from the lead-in portion of the Phase 2 study which demonstrated that oral seliciclib could be safely administered in two dosing schedules which were well tolerated and met the criteria for proceeding to the randomized stage of the study. Seliciclib treatment resulted in prolonged stable disease in 70% of previously-treated NPC patients, including 3 with stable disease lasting longer than 8 months, suggesting seliciclib inhibits tumor growth in NPC. The data support further clinical development of oral seliciclib in NPC.

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, now completed, 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 pharmacokinetic and pharmacodynamic effects of the drug and document anti-tumor activity. Aurora kinases, or AK, are a family of serine/threonine protein kinases discovered by Professor David Glover, our Chief Scientist, which 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. 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. Further work on CYC116 will be undertaken when appropriate levels of resource are available to direct to the program.

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CYC065

In December 2010, at the ASH conference, we announced the presentation of new preclinical data for CYC065, a novel, orally-available, cell cycle kinase inhibitor currently in IND-directed development. CYC065 and other compounds in a related series target the same key CDK/cyclin complexes which are targeted by seliciclib. CYC065 retains the specificity and mechanism of action of seliciclib, but has increased anti-proliferative potency and improved pharmaceutical properties.

The data was presented by Noopur Raje, M.D., Director of the Center for Multiple Myeloma at Massachusetts General Hospital Cancer Center in Boston and Associate Professor of Medicine at Harvard Medical School. Dr. Raje and colleagues presented results of a study entitled, CYC065, a Potent Derivative of Seliciclib Is Active In Multiple Myeloma In Preclinical Studies . The data demonstrate that CYC065 is cytotoxic at sub-micromolar concentrations against myeloma cell lines and CD138+ myeloma cells derived from patients. CYC065 demonstrated antiproliferative activity even in the presence of the growth stimulatory effects of both cytokines and bone marrow stromal cells. CYC065 induced apoptosis in myeloma cells as evidenced by the appearance of cleaved PARP.

Cyclacel discovered CYC065 and other novel CDK inhibitors in collaboration with the Cancer Research UK Centre for Cancer Therapeutics at The Institute of Cancer Research (ICR), London, UK.

Other programs

We have allocated limited resources to other programs allowing us to maintain and build on our core competency in cell cycle biology and related drug discovery. In our second generation CDK inhibitor program, we have discovered several series of CDK inhibitors that we believe may prove to be more potent anticancer agents than seliciclib based on preclinical observations. In our polo-like kinase or Plk inhibitor program we have discovered potent and selective small molecule inhibitors of Plk1, a kinase active during cell division, targeting the mitotic phase of the cell cycle. Plk was discovered by Professor David Glover, our Chief Scientist. The Company has a number of earlier stage programs for which limited or no resources will be allocated. For example, extensive preclinical data published by independent investigators evidence activity by our CDK inhibitors, including seliciclib, in various autoimmune and inflammatory diseases and conditions associated with aberrant cell proliferation including glaucoma, graft-versus-host disease, idiopathic pulmonary fibrosis, lupus nephritis, polycystic kidney disease and rheumatoid arthritis. In our GSK-3 inhibitor program we have demonstrated evidence of activity in preclinical models of Type 2 Diabetes.

Where appropriate we intend to progress such programs through collaboration with groups that specialize in the particular disease area until such times that these programs can be partnered and/or progressed should funding become available.

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 classes capable of breaking the binding between p53 and Hdm2.

Cyclin Binding Groove Inhibitors

The activity of CDK can be inhibited by various methods, such as by blocking the ATP site, as is the case with seliciclib, or by inhibiting the substrate binding site on the associated 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.

Non-oncology Programs

Cell Cycle Inhibitors in Autoimmune & Inflammatory Diseases

Preclinical results from several independent investigators suggest that cell cycle inhibitors such as seliciclib and its backup molecules arrest the progress of the cell cycle and may have therapeutic benefit in the treatment of patients with autoimmune and inflammatory diseases as well as in diseases characterized by uncontrolled cell proliferation. Published data indicate potential benefit in graft-versus-host disease, idiopathic pulmonary fibrosis,

glomerulonephritis, lupus nephritis, polycystic kidney disease and rheumatoid arthritis.

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 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 rely on 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 with antiviral potency equivalent to some existing HIV/AIDS therapeutic agents. We intend to progress this program through collaboration with groups that specialize in virology research.

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GSK-3 Inhibitors in Type 2 Diabetes

Inhibition of Glycogen Synthase Kinase-3 or GSK-3, downstream of insulin action, is an essential element in the body s regulation of blood sugar, and is a recognized target for the treatment of Type 2 diabetes. GSK-3 is a serine/threonine protein kinase 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 obese 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.

Commercial Products

We have 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.

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 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.

Legal Proceedings

From time to time, we may be involved in routine litigation incidental to the conduct of our business. On April 27, 2010, we were served with a complaint filed by Celgene Corporation in the United States District Court for the District of Delaware seeking a declaratory judgment that four of our own patents, claiming the use of romidepsin injection in T-cell lymphomas, are invalid and not infringed by Celgene s products, but directly involve the use and administration of Celgene s ISTODAX® (romidepsin for injection) product. On June 17, 2010, we filed our answer and counterclaims to the declaratory judgment complaint. We have filed counterclaims charging Celgene with infringement of each of our four patents and seeking damages for Celgene s infringement as well as injunctive relief. The four patents directly involve the use and administration of Celgene s ISTODAX® (romidepsin for injection) product.

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 marketing, medical and regulatory functions are

located. Our research facility is located in Dundee, Scotland, which is also the center of our translational work and development programs.

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THE OFFERING

Common stock covered hereby	Up to 100,000 shares of our common stock to be offered for resale by the selling stockholder following issuance upon exercise of the amended and restated warrant.
Common stock outstanding as of May 24, 2011	46,603,321 shares
Use of proceeds	We may receive proceeds in connection with the exercise of the amended and restated warrant, if and when exercised by Kingsbridge. However, we cannot predict the timing or the amount of the exercise of this warrant. Any proceeds we may receive will be used by us for general corporate purposes, including capital expenditures, the advancement of our drug candidates in clinical trials, such as our SEAMLESS pivotal Phase 3 trial of oral sapacitabine, and to meet working capital needs. The amounts and timing of the expenditures will depend on numerous factors, such as the timing and progress of our clinical trials and research and development efforts, technological advances and the competitive environment for our drug candidates. We expect from time to time to evaluate the acquisition of businesses, products and technologies for which a portion of the net proceeds may be used, although we currently are not planning or negotiating any such transactions. As of the date of this Prospectus, we cannot specify with certainty all of the particular uses for the net proceeds to us from the the exercise of the warrant by Kingsbridge. Accordingly, we will retain broad discretion over the use of these proceeds, if any.
Risk factors	The shares of common stock offered hereby involve a high degree of risk. See Risk Factors beginning on page 9.
Dividend policy	We currently intend to retain any future earnings to fund the development and growth of our business. Therefore, we do not currently anticipate paying cash dividends on our common stock.
Trading Symbol	Our common stock currently trades on the NASDAQ Global Market under the symbol CYCC.

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RISK FACTORS

Any investment in our common stock involves a high degree of risk. Investors should carefully consider the risks described below, together with all of the other information included in this Prospectus, before deciding whether to purchase shares of our common stock. 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. This Prospectus also contains forward-looking statements that involve risks and uncertainties. Our operating results could differ materially from those anticipated in these forward-looking statements as a result of certain risk factors, including the risks we face as described below and elsewhere in this Prospectus.

Risks Associated with Development and Commercialization of our Drug Candidates

Clinical trial designs that were discussed with the authorities prior to their commencement may subsequently be considered insufficient for approval at the time of application for regulatory approval. Thus, our SPA regarding our SEAMLESS trial does not guarantee marketing approval or approval of our sapacitabine oral capsules for the treatment of acute myeloid leukemia.

On September 13, 2010, we reached agreement with the FDA regarding an SPA on the design of a pivotal Phase 3 trial for our sapacitabine oral capsules as a front-line treatment in elderly patients aged 70 years or older with newly diagnosed acute myeloid leukemia, or AML, who are not candidates for intensive induction chemotherapy, or the SEAMLESS trial. An SPA provides trial sponsors with an agreement from the FDA that the design and analysis of the trial adequately address objectives in support of a submission for a marketing application if the trial is performed according to the SPA. The SPA may only be changed through a written agreement between the sponsor and the FDA or if the FDA becomes aware of a substantial scientific issue essential to product efficacy or safety. On January 11, 2011, we opened enrollment of the SEAMLESS trial.

An SPA, however, neither guarantees approval nor provides any assurance that a marketing application would be approved by the FDA. There are companies that have been granted SPAs but have ultimately failed to obtain final approval to market their drugs. The FDA may revise previous guidance or decide to ignore previous guidance at any time during the course of clinical activities or after the completion of clinical trials. The FDA may raise issues relating to, among other things, safety, study conduct, bias, deviation from the protocol, statistical power, patient completion rates, changes in scientific or medical parameters or internal inconsistencies in the data prior to making its final decision. The FDA may also seek the guidance of an outside advisory committee prior to making its final decision. Even with successful clinical safety and efficacy data, including such data from a clinical trial conducted pursuant to an SPA, we may be required to conduct additional, expensive clinical trials to obtain regulatory approval.

The development program for our lead drug candidate sapacitabine is based, in part, on intellectual property rights we license from others and any termination of this license could seriously harm our business.

Pursuant to the Daiichi-Sankyo license under which we license certain patent rights for sapacitabine, our lead drug candidate, we are required 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, unless we are prevented from doing so by virtue of an exceptional cause, which generally constitutes a scientific or other technical cause outside of our control or arising from the activities of third parties, difficulties outside of our reasonable control in patient recruitment into trials or any significant, unexpected change in the regulatory requirements in a country affecting the development of our drug candidate. If regulatory approval is not obtained by September 2011, and there has been no exceptional cause responsible for the delay, the agreement provides that Daiichi-Sankyo may terminate the license. As it is unlikely that regulatory approval for the product will be obtained by September 2011 it is the Company s intention to negotiate an appropriate amendment to this date on various grounds, among other things, changes that have taken place in the regulatory environment, as provided within the agreement. If negotiation was not successful, litigation could ensue and there would be no assurances as to the result thereof. Termination of the license agreement could seriously harm our business. On termination, if Daiichi-Sankyo wishes to acquire an exclusive license to sapacitabine 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.

In general, the license may be terminated by us for technical, scientific, efficacy, safety, or commercial reasons on six months notice, or twelve months if after a launch of a sapacitabine-based product, or by either party for material default.

Although we are currently in compliance with all of our material obligations under this license, if we were to breach any such obligations, our counterparty may be entitled to terminate the license. This would restrict or delay or eliminate our ability to develop and commercialize these drug candidates, which could adversely affect our business.

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.

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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.

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

Clinical trials are expensive, complex can take many years to conduct and may 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;
- uncertain dosing issues may or may not be related to suboptimal pharmacokinetic and pharmacodynamic behaviors;
- 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, neutropenia and gastro-intestinal toxicity were observed in patients receiving sapacitabine and elevations of liver enzymes and decrease in potassium levels have been observed in patients receiving seliciclib.

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.

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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.

Our development of small molecule inhibitors of CDK and AK is based on our understanding of the mechanisms of action of CDK and AK inhibitors and their interaction with other cellular mechanisms. One of our drug candidates, seliciclib, is a CDK inhibitor, and CYC116 is an AK and VEGFR2 inhibitor. 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. If our understanding of the role played by CDK or AK inhibitors in regulating the cell cycle is incorrect, seliciclib and/or CYC116 may fail to produce therapeutically relevant results hindering our ability to pursue our clinical and regulatory strategy.

We are making 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 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, data management companies, 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;
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.

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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 and will be required to secure alternative third-party suppliers to our current suppliers. 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 our current or future 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 or are unable to secure alternative third-party suppliers to our current suppliers, the drug development, regulatory approval or commercial launch of any related drugs may be delayed or blocked 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, control and regulatory capabilities and develop financial, 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 wherever 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. The success of the commercialization of the ALIGN products depends, in large part, on our continued ability to develop and maintain important relationships with 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.

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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 pivotal or suitable for registration late Phase 2 or 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 the FDA and other applicable foreign and U.S. regulatory requirements may subject us 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 the 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 adoption of new regulations requiring new or different evidence of safety and efficacy for the intended use of a drug candidate.

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 which was 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.

A large number of drug candidates are in development for the treatment of leukemia, lung cancer, lymphomas and nasopharyngeal cancer. Several pharmaceutical and biotechnology companies have nucleoside analogs or other products on the market or in clinical trials which may be competitive to sapacitabine in both hematological and oncology indications. These include Celgene, Cephalon, Eisai, Johnson & Johnson, Eli Lilly, Genzyme, GlaxoSmithKline, Hospira, Pfizer, Seattle Genetics, Sunesis and Vion. There are two other-orally available CDK inhibitor in Phase 2 clinical trials. PD-0332991 (Pfizer/Onyx) and PHA-848125 (Nerviano Medical Sciences) target different subsets of CDK enzymes and have a different mechanism of action from seliciclib. We believe that seliciclib is currently the most advanced orally available CDK-specific agent in Phase 2 clinical trials but that there are a number of companies, including AstraZeneca, Bayer-Schering, Eisai, Merck, Nerviano Medical Sciences, Pfizer, Piramal Life Sciences, and Roche that 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, or CTEP, is continuing to enroll patients in a CTEP sponsored trial 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, Entremed, Merck, jointly with Vertex, Nerviano Medical Sciences, Pfizer, Rigel, Sunesis and Takeda-Millennium have commenced Phase 1 or Phase 2 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, Nerviano Medical Sciences, Onconova, Takeda-Millennium and Tekmira Pharmaceuticals Corporation have commenced Phase 1 or Phase 2 clinical trials with Plk inhibitor candidates for oncology indications. 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.

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 candid