

Cyclacel Pharmaceuticals, Inc.
Form S-1
December 26, 2012
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As filed with the Securities and Exchange Commission on December 26, 2012

Registration No. 333-

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

FORM S-1

**REGISTRATION STATEMENT
UNDER THE SECURITIES ACT OF
1933**

CYCLACEL PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

91-1707622
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)

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

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Approximate date of commencement of proposed sale to public: From time to time after the effective date of this registration statement.

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, check the following box:

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:

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

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(d) under the Securities Act, check the following box:

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

Accelerated filer

Non-accelerated filer

Smaller reporting company

(Do not check if a smaller reporting company)

CALCULATION OF REGISTRATION FEE

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Title of Each Class of Security Being Registered	Amount Being Registered(1)	Proposed Maximum Offering Price Per Security	Proposed Maximum Aggregate Offering Price	Amount of Registration Fee
Shares of common stock, \$.001 par value	1,689,317	\$ 6.19(2)	\$ 10,456,872.23	\$ 1,426.32

(1) Pursuant to Rule 416 under the Securities Act of 1933, as amended (the **Securities Act**), this Registration Statement shall also cover any additional shares of common stock which become issuable by reason of any stock dividend, stock split or other similar transaction effected without the receipt of consideration that results in an increase in the number of the outstanding shares of common stock of the registrant.

(2) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(c) under the Securities Act, based upon the average of the high and low prices of the common stock on The NASDAQ Global Market on December 18, 2012. Under a common stock purchase agreement, Aspire Capital Fund, LLC has agreed to purchase up to \$20.0 million of shares of the Registrant's common stock.

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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The information in this prospectus is not complete and may be changed. The selling securityholders 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 state where the offer or sale is not permitted.

Subject to Completion, dated December 26, 2012

PROSPECTUS

**Relating to the Sale of up to
1,689,317 Shares of Common Stock, \$0.001 Par Value**

CYCLACEL PHARMACEUTICALS, INC.

This prospectus relates to the sale of up to 1,689,317 shares of our common stock by Aspire Capital Fund, LLC. Aspire Capital is also referred to in this prospectus as the selling stockholder. The prices at which the selling stockholder may sell the shares will be determined by the prevailing market price for the shares or in negotiated transactions. We will not receive proceeds from the sale of the shares by the selling stockholder. However, we may receive gross proceeds of up to \$20,000,000 from the sale of our common stock the selling stockholder, pursuant to a common stock purchase agreement entered into with the selling stockholder on December 14, 2012, once the registration statement, of which this prospectus is a part, is declared effective.

The selling stockholder is an underwriter within the meaning of the Securities Act of 1933, as amended. We will pay the expenses of registering these shares, but all selling and other expenses incurred by the selling stockholder will be paid the selling stockholder.

Our common stock is listed on the NASDAQ Global Market under the symbol CYCC. On December 21, 2012, the last reported sale price for our common stock was \$5.71 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 12 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 December 26, 2012.

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PART II INFORMATION NOT REQUIRED IN PROSPECTUS	

You should rely only on the information provided in this Prospectus or in any free writing Prospectus prepared by or on behalf of us or to which we have referred you. 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, 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 12.

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 Company

We are a biopharmaceutical business dedicated to the discovery, development and commercialization of novel, mechanism-targeted drugs to treat cancer and other serious diseases. We are focused on delivering leading edge therapeutic management of cancer patients based on a clinical development pipeline, led by sapacitabine, of novel drug candidates. Our core area of expertise, and a foundation of the Company since our inception, is in cell cycle biology; 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 focusing our clinical development priorities on:

- Sapacitabine in acute myeloid leukemia, or AML, in elderly patients;
- Sapacitabine in myelodysplastic syndromes, or MDS, in older patients; and
- Sapacitabine in 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 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 SEAMLESS trial. SEAMLESS is a registration-directed, clinical trial of sapacitabine oral capsules is being conducted under the SPA and is a randomized study against an active control drug with the primary efficacy of overall survival.

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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 CYC065.

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.

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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. Over 500 patients have received sapacitabine in Phase 2 studies in AML, MDS, CTCL and NSCLC and Phase 1 studies in hematological malignancies and solid tumors. Sapacitabine, an orally-available nucleoside analogue, is currently being studied in SEAMLESS, an ongoing, Phase 3, registration-directed trial in elderly patients aged 70 years or older with newly diagnosed AML who are not candidates for or have refused induction chemotherapy. SEAMLESS will be conducted under a SPA.

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

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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.

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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.

In November 2012, the results from the Phase 2 study were published in *The Lancet Oncology*, demonstrating the safety and efficacy of sapacitabine in this patient population. The Phase 2 study enrolled and treated between December 27, 2007 and April 21, 2009, a total of 105 patients aged 70 years or above with untreated or first relapse AML. The median age of patients was 77 years (range 70–91). The group was comprised of a randomized cohort of 60 patients and an expanded, non-randomly assigned cohort enrolling a further 45 patients. Of the 105 patients, 86 were previously untreated and 19 in first relapse. Approximately 50% of patients had AML de novo and 50% had AML preceded by antecedent hematological disorder (AHD), such as MDS or myeloproliferative disease, or treatment-related AML. All but one enrolled patients had intermediate or unfavorable cytogenetics. The randomized cohort of patients were randomly assigned to one of three dosing schedules: 200 mg twice a day for 7 days (group A); 300 mg twice a day for 7 days (group B); and 400 mg twice a day for 3 days each week for 2 weeks (group C). All schedules were given in 28 day cycles. The 3-day dosing schedule in group C was selected for further clinical development in elderly patients with untreated AML. This decision was based on the schedule's overall efficacy profile, which included a 1-year survival rate of 30%, median overall survival of 213 days and durable complete remissions (CRs) in 25% of patients. The median overall survival of patients from all groups who achieved CR was 525 days (95% C.I. 192–798). The most common grade 3–4 adverse events regardless of causality were anemia, neutropenia, thrombocytopenia, febrile neutropenia and pneumonia. Seven deaths were thought to be probably or possibly related to sapacitabine treatment. Approximately 31% of all patients received sapacitabine for at least 4 cycles.

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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 June 2010, at the American Society of Clinical Oncology, or ASCO, meeting we reported interim response data for the ongoing Phase 2 clinical trial of sapacitabine in older patients with MDS. The study has recently completed enrollment of 61 patients aged 60 or older with MDS who were previously treated with azacitidine or decitabine or both. In this three-arm study, Arms B & C enrolled 20 patients each while Arm A enrolled 21 patients across the same three randomized dosing schedules of sapacitabine tested in the AML stratum of the study. All patients have received at least one hypomethylating agent and 15 patients (25%) have received two hypomethylating agents, i.e., azacitidine and decitabine. Approximately 51% of the 61 patients had baseline bone marrow blast counts above 10%. Based on interim data, the overall response rate is 24% on Arm A, the 7-day low dose schedule, 35% on Arm B, the 7-day high dose schedule, and 10% on Arm C, the 3-day high dose schedule. Two patients achieved complete remission and both were treated on Arm A. Thirty-day mortality from all-causes is 4.8% on Arm A, 0% on Arm B and 15% on Arm C. Approximately 34% of the patients received 4 or more cycles of sapacitabine.

In October 2012, at the The Eighth Annual Hematologic Malignancies 2012 Conference, we reported updated data from an ongoing, multicenter, Phase 2 randomized trial of sapacitabine in older patients with intermediate-2 or high-risk MDS after treatment failure of front-line hypomethylating agents, such as azacitidine (Vidaza®) and/or decitabine (Dacogen®). Median overall survival to date for all 63 patients in the Phase 2 study is 252 days or approximately 8 months. Median overall survival for 41 out of 63 patients with 10% or more blasts in their bone marrow is 274 days or approximately 9 months. Updated median survival for all three arms is 252 days (approximately 8 months). The median survival for each arm is 291 days (approximately 10 months) for Arm G, 274 days (approximately 9 months) for Arm H, and 227 days (approximately 8 months) for Arm I. Twenty-seven percent of all patients received 6 or more cycles. Twenty-two percent of patients are still alive and longer follow-up is needed to assess 1-year survival and overall survival of each arm.

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 September 13, 2010, we announced that we reached agreement with the FDA regarding the SPA, on the design of a pivotal Phase 3 trial, the SEAMLESS trial, for our 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. SEAMLESS is being conducted under an SPA agreement that Cyclacel reached with the FDA. Patients who received hypomethylating agents for prior myelodysplastic syndromes or myeloproliferative diseases are excluded from SEAMLESS. Patients in the control arm of SEAMLESS will receive decitabine alone, while in the experimental arm of SEAMLESS, patients will receive intravenous decitabine at 20 mg/m² per day for five consecutive days of a 4-week cycle (odd cycles) alternating with sapacitabine at 300 mg orally twice per day for three days per week for two weeks of a 4-week cycle (even cycles). The primary efficacy endpoint is overall survival. A prespecified interim analysis for futility will be performed and reviewed by the Data Safety Monitoring Board. 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.

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In December 2012, at the 54th Annual Meeting of ASH, the Company announced updated survival data from the pilot study and lead-in phase of SEAMLESS. Forty-six patients were treated with alternating cycles of sapacitabine and decitabine, which is the treatment regimen in the experimental arm of SEAMLESS. Median age is 77 years (range 70-90). Thirty-three patients (72%) are 75 years or older. Median overall survival is 238 days, or approximately 8 months. The number of patients still alive at 3 months was 38 (83%), at 6 months 30 (65%), at 12 months 16 (35%) and at 18 months 12 (26%). Sixteen patients (35%) survived 1 year or longer. Among 33 patients who are 75 years or older, median overall survival is 263 days, or approximately 9 months, and 1-year survival is 36%. Nineteen patients (41%) responded with 10 complete responses (CRs), 4 partial responses (PRs) and 5 major hematological improvements (HIs). Median time to response is 2 cycles, i.e., one cycle of decitabine and one cycle of sapacitabine (range 1-10). Twenty-seven patients (59%) received 5 or more cycles of treatment. Two dose-limiting toxicities (DLT) were observed (lung infection/sepsis, typhlitis). Thirty-day mortality from all causes was 4%. Sixty-day mortality from all causes was 13% with one death from typhlitis considered to be possibly related to decitabine by investigator assessment. The sequential combination of decitabine and sapacitabine is safe and active.

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

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.

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, the opportunity to apply for grant funding from the U.S. 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

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/E, CDK2/A, 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.

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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, suggests that seliciclib treatment neither aggravated the known toxicities of standard first and second-line chemotherapies nor appeared to cause unexpected toxicities, although these trials were not designed to provide statistically significant comparison.

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. APPRAISE was led by Chandra P. Belani, M.D. at Milton S. Hershey Medical Center, Penn State University. 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, or OS, 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.

Published pre-clinical work indicated that K-Ras mutational status, cyclin D1 and cyclin E1 protein levels correlated strongly with tumor sensitivity towards seliciclib. In order to explore this possible molecular rationale for the difference in OS, we retrospectively collected and analyzed available biopsy samples from APPRAISE patients who granted informed consent. As only 30 patient samples were available from the 152 APPRAISE patients who gave consent, results of the retrospective analysis were insufficient to allow meaningful correlation. A new prospectively designed study is required to test the hypothesis that these biomarkers can predict therapeutic effect of seliciclib in patients with advanced stage NSCLC.

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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.

CYC065

CYC065 is a novel, orally available, cell cycle kinase inhibitor currently in IND-directed preclinical development. CYC065 targets similar CDK/cyclin complexes to those targeted by seliciclib, our first generation CDK inhibitor currently in Phase 2 studies. CYC065 retains the high CDK specificity of seliciclib, but with substantially higher anti-proliferative potency and improved pharmaceutical properties. CYC065 is a second generation aminopurine which selectively inhibits CDK2, CDK5 and CDK9. Strong preclinical anti-cancer efficacy data for CYC065 in multiple myeloma, chronic lymphocytic leukemia (CLL) and mixed lineage leukemia (MLL) have been presented at the 2010 Annual Meetings of the American Society of Hematology (ASH) 1 and the American Association of Cancer Research (AACR). 2 3 At the 2010 AACR CYC065 was also reported to be active in solid tumor models, including trastuzumab-resistant, cyclin E overexpressing breast cancer. These findings were subsequently published by Scaltriti, et al (Cyclin E amplification/overexpression is a mechanism of trastuzumab resistance in HER2+ breast cancer patients , PNAS, 2011:108:3761-3766). In addition CYC065 was shown to have preclinical efficacy in proliferative kidney disease models (Cyclacel data on file). Cyclacel discovered CYC065 in collaboration with the Cancer Research UK Centre for Cancer Therapeutics at The Institute of Cancer Research. In November 2012, we received a grant of approximately \$1.9 million from the UK Government s Biomedical Catalyst to complete investigational new drug (IND)-directed preclinical development of CYC065.

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, 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. VEGFR2 is a receptor protein that plays a key regulatory role in the angiogenesis pathway, or blood vessel formation. VEGFR is targeted by recently

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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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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. Our polo-like kinase or Plk inhibitor program targets the mitotic phase of the cell cycle with the objective of identifying potent and selective small molecule inhibitors of 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 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 of aberrant cell proliferation including glaucoma, lupus nephritis, idiopathic pulmonary fibrosis, 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 mechanism of action or disease area until such times that these programs can be partnered and/or progressed should funding become available.

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 translational work and development programs.

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THE OFFERING

Common stock covered hereby: Up to 1,689,317 shares, including 233,440 shares currently outstanding

**Common stock outstanding as of
December 18, 2012:**