

Cyclacel Pharmaceuticals, Inc.  
Form 424B3  
April 30, 2013  
Table of Contents

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Registration No. 333-170421

## PROSPECTUS

**Relating to the Resale of up to  
624,445 Shares of Common Stock, \$0.001 Par Value,  
Comprised of: (i) 29,932 Shares of Common Stock; and  
(ii) up to 594,513 Shares of Common Stock  
Issuable upon Exercise of Outstanding Warrants**

### CYCLACEL PHARMACEUTICALS, INC.

This prospectus relates to the resale or other disposition of 624,445 shares of common stock, par value \$0.001 per share, by the selling stockholders identified herein, (i) 29,932 of which are issued and outstanding; and (ii) 594,513 of which are issuable upon exercise of five-year warrants to purchase common stock at an exercise price of \$13.44 per share (the **Warrants**) that we issued as part of a private placement of our securities on October 7, 2010 (the **Private Placement**).

The share amounts and prices included herein give effect to the one-for-7 reverse stock split of our common stock, which became effective on August 24, 2012.

For a list of the selling stockholders, please refer to the section entitled **Selling Stockholders** of this prospectus. The shares may be sold or otherwise disposed of from time to time by the selling stockholders. 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 stockholders. We will not receive any proceeds from the sale or other disposition of common stock by the selling stockholders. However, to the extent that the Warrants are exercised for cash, we will receive the payment of the exercise price in connection with such exercise.

Our common stock is listed on the NASDAQ Global Market under the symbol **CYCC**. On April 12, 2013, the last reported sale price for our common stock was \$5.13 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 11 before**

**deciding whether to invest in our securities.**

**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 April 30, 2013.

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Table of Contents

TABLE OF CONTENTS

	Page
<u>PROSPECTUS SUMMARY</u>	1
<u>THE OFFERING</u>	10
<u>RISK FACTORS</u>	11
<u>SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS</u>	36
<u>USE OF PROCEEDS</u>	36
<u>PLAN OF DISTRIBUTION</u>	37
<u>DESCRIPTION OF SECURITIES</u>	40
<u>DISCLOSURE OF COMMISSION POSITION ON INDEMNIFICATION FOR SECURITIES ACT LIABILITIES</u>	59
<u>MARKET FOR COMMON EQUITY AND RELATED STOCKHOLDER MATTERS</u>	60
<u>LEGAL MATTERS</u>	61
<u>EXPERTS</u>	61
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	61
<u>INCORPORATION OF DOCUMENTS BY REFERENCE</u>	61

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 61. 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.

Table of Contents

**PROSPECTUS SUMMARY**

The following is a summary of what we believe to be the most important aspects of our business and the offering of our securities under this prospectus. We urge you to read this entire prospectus, including the more detailed consolidated financial statements, notes to the consolidated financial statements and other information incorporated by reference from our other filings with the SEC or included in any applicable prospectus supplement. Investing in our securities involves risks. Therefore, carefully consider the risk factors on page 11 of this prospectus and in any prospectus supplements and in our most recent annual and quarterly filings with the SEC, as well as other information in this prospectus and any prospectus supplements and the documents incorporated by reference herein or therein, before purchasing our securities. Each of the risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities.

**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*

***Oncology Development Programs***

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

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

The U.S. Food and Drug Administration, or FDA, and the European Medicines Agency, or EMA, have designated sapacitabine as an orphan drug for the treatment of both AML and MDS.

We are currently evaluating sapacitabine in a Phase 3 study being conducted under a Special Protocol Assessment, or SPA, with the FDA for the front-line treatment of AML in the elderly. We are also exploring sapacitabine in Phase 2 studies for MDS, NSCLC and chronic lymphocytic leukemia, or CLL, and in a Phase 1 study in solid tumors in combination with our own drug candidate, seliciclib.

In our second development program, we are evaluating cyclin dependent kinase, or CDK, inhibitors. CDKs are involved in cancer cell growth, metastatic spread and DNA damage repair. Seliciclib, our lead CDK inhibitor, 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. In breast and lung tumors, overexpression of cyclin E is associated with poor prognosis and drug resistance. Resistant breast and lung tumor cell lines overexpressing cyclin E are resensitized to apoptotic cell killing by seliciclib. NSCLC cell lines with Ras-activating mutations, such as KRAS and NRAS, have been found to be sensitive to seliciclib-induced apoptosis. 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. Seliciclib has completed a Phase 2B randomized study in third-line NSCLC and is currently undergoing a study in solid tumors in combination with our own drug candidate, sapacitabine.

Table of Contents

Our second generation CDK inhibitor, CYC065, is a highly selective inhibitor of CDK s targeting CDK -2, -5 and -9 enzymes. CYC065 has shown to have increased anti-proliferative potency and improved pharmaceutical properties compared to seliciclib. Investigational new drug (IND)-enabling studies with CYC065 are in progress supported by a \$1.9 million grant from the UK Government s Biomedical Catalyst.

In addition to these development programs, we have allocated limited resources, if the funds are available, to other programs allowing us to maintain and build on our core competency in cell cycle biology and related drug discovery. 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, and CYC116, an orally-available inhibitor of Aurora kinase, or AK, A and B and Vascular Endothelial Growth Factor Receptor 2, or VEGFR2, has completed a multicenter Phase 1 trial.

We also have a number of earlier stage programs for which limited or no resources will be allocated in the foreseeable future. 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 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.

*Sapacitabine*

Sapacitabine (previously known as CYC682) is an orally-available nucleoside analogue. Both sapacitabine and CNDAC, its major metabolite, have demonstrated potent anti-tumor activity in preclinical studies. 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 novel mechanism whereby the compound interferes with DNA synthesis through the incorporation of CNDAC into DNA during replication or repair, triggering a b-elimination reaction and leading to the formation of SSBs, which can activate the G2 checkpoint transcription coupled nucleotide excision repair, or TC-NER. During subsequent rounds of replication, SSBs are converted to double-strand breaks (DSBs); these can be repaired by the homologous recombination repair (HRR) pathway, or, if unrepaired, result in cell death.

We are currently exploring sapacitabine in both hematological cancers and solid tumors and over 500 patients have received sapacitabine in Phase 1, 2 and 3 studies.

Table of Contents

*Hematological Cancers*

*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*

The SEAMLESS study is being conducted under an SPA agreement that Cyclacel reached with the FDA. SEAMLESS builds on promising one 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 two treatment arms. In Arm A, sapacitabine is administered in alternating cycles with decitabine and in Arm C decitabine is administered alone. The primary efficacy endpoint is overall survival and the study is designed to demonstrate an improvement in overall survival. Approximately 242 patients per arm, or a total of 485 patients from approximately 50 centers, will be enrolled. The SEAMLESS study is designed to have a 90% probability of detecting a 27.5% difference in overall survival and a prespecified interim analysis for futility will be performed and reviewed by the Data Safety Monitoring Board, or DSMB. In addition, the DSMB will periodically convene to review data for safety or efficacy from each approximately 100 patients enrolled.

In December 2012, the DSMB met and recommended that the study should continue as planned after reviewing available data from 119 randomized patients. The DSMB noted that no safety or efficacy concerns were identified. Results from an on-going, multicenter, Phase 1/2 clinical trial examining the safety and efficacy of oral sapacitabine administered sequentially with decitabine, the same treatment regimen as Arm A in SEAMLESS, was reported during a poster session at the 2012 American Society of Hematology, or ASH, Annual Meeting in Atlanta, Georgia. Forty-six patients were treated with alternating cycles of sapacitabine and decitabine. Median age was 77 years (range 70-90). Thirty-three patients (72%) were 75 years or older. Median overall survival was 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 were 75 years or older, median overall survival was 263 days, or approximately 9 months, and 1-year survival was 36%. Nineteen patients (41%) responded with 10 complete responses (CRs), 4 partial responses (PRs) and 5 major hematological improvements (HIs). Median time to response was 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.

*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, had 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 were to assess complete remission, or CR, 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 one year survival rate in the event that all three dosing schedules are active.



Table of Contents

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.

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

In September 2008, we advanced sapacitabine into an open-label, multi-center, randomized Phase 2 trial as a second-line treatment in patients aged 60 or older with intermediate-2 or high-risk MDS after treatment failure of front-line hypomethylating agents, such as azacitidine and/or decitabine. The Phase 2 study randomized 63 patients aged 60 years or older with MDS of intermediate-2 (n=52) or high-risk (n=11) classification by the International Prognostic Scoring System (IPSS) at study entry to receive sapacitabine every 4 weeks on one of 3 dosing schedules: 200 mg twice daily for 7 days (Arm G), 300 mg once daily for 7 days (Arm H), or 100 mg once daily for 5 days per week for 2 weeks (Arm I). The primary efficacy endpoint of the study is 1-year survival 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. All patients in the study progressed after receiving azacitidine, decitabine, or both agents. 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.

In October 2012, at The Eighth Annual Hematologic Malignancies 2012 Conference, we reported updated data from the ongoing Phase 2 trial. Median overall survival to date for all 63 patients in the study was 252 days or approximately 8 months. Median overall survival for 41 out of 63 patients with 10% or more blasts in their bone marrow was 274 days or approximately 9 months. Updated median survival for all three arms was 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 were still alive and longer follow-up is needed to assess 1-year survival and overall survival of each arm.

Table of Contents

Median survival for patients with intermediate-2 or high-risk disease, as defined by the International Prognostic Scoring System (IPSS), is 4.3 to 5.6 months as reported in literature. Patients with high IPSS scores also have a high probability of experiencing transformation of their MDS into AML, an aggressive form of blood cancer with typically poor survival.

*Solid Tumors*

*Phase 2 clinical trial in patients with NSCLC*

We are evaluating sapacitabine in 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, one year survival, overall survival and safety.

Forty-eight patients have been treated with two dosing schedules, either twice daily or once a day. In the twice daily schedule 15 patients were treated with escalating doses. The recommended Phase 2 dose was reached at 75 mg twice daily for 5 days per week for 2 weeks every 3 weeks. Among 12 patients treated at this recommended Phase 2 dose, 4 achieved stable disease. All 4 responders had at least 2 prior therapies and have been discontinued from the study. Responders received an average of 7 treatment cycles.

In the once daily schedule, 33 patients were treated with escalating doses. Maximum tolerated dose has not been reached at the upper limit of the dosing range as per protocol. Patients are currently being entered into the 200 mg once daily dosing level for 5 days per week for 2 weeks every 3 weeks. Among 25 patients treated with daily doses ranging from 100 mg to 175 mg, two patients achieved PR and 10 stable disease. The two PR responders had 3 or 4 prior therapies, respectively, and one remains on study. Among the 10 stable disease responders, 9 had at least 2 prior therapies and 2 remain on study. Responders received an average of 10 treatment cycles.

*Phase 1 clinical trial of sapacitabine and seliciclib in patients with advanced cancers*

In an open label Phase 1, single-arm dose escalation study, sapacitabine and seliciclib were administered sequentially in patients with incurable advanced solid tumors unresponsive to conventional treatment or for which no effective therapy exists. Sapacitabine was dosed twice daily for 7 days (Day 1-7) and seliciclib twice daily for 3 days (Day 8-11). One treatment cycle is three weeks. At least 3 patients were enrolled at each escalating dose level. The first tumor imaging study is conducted after 2 cycles of treatment and every 3 cycles thereafter. The primary objective of the study is to determine the maximum tolerated dose, or MTD, and recommended Phase 2 dosing schedule of sapacitabine and seliciclib administered sequentially. The secondary objective was to evaluate the antitumor activity of sequential treatment and to explore the pharmacodynamic effect of this treatment in skin and peripheral blood mononuclear cells. We reported at the 2012 American Society of Clinical Oncology Annual Meeting that 34 heavily-pretreated patients with advanced solid tumors had been treated with escalating doses. The MTD for sequential administration of sapacitabine and seliciclib was reported as sapacitabine 50 mg twice daily followed by seliciclib 1200 mg twice daily. Pharmacodynamic effects of sapacitabine and seliciclib were observed in skin biopsies showing a 2.3-fold increase in H2AX staining post-sapacitabine and a further 0.58-fold increase post-seliciclib.



Table of Contents

Among 19 patients treated at the MTD, 3 partial responses (PR) occurred in patients with breast, ovarian and pancreatic cancer and 1 stable disease in a patient with ovarian cancer. Thirteen out of the 19 patients are BRCA-mutation carriers, in their germ line. Stable disease was achieved in 6 additional patients treated with the other dosing schedules. The number of treatment cycles administered ranges from 2 to over 15 cycles. The breast cancer patient who achieved PR remains on study with over 15 cycles and both ovarian cancer patients remain on study with over 2 and 12 cycles, respectively.

BRCA1 and BRCA2, or breast cancer susceptibility genes, are tumor suppressor genes that help ensure the stability of DNA, the cell's genetic material, and help prevent uncontrolled cell growth. Genetic testing for BRCA-status is routinely available. BRCA mutation has been linked to predisposition to breast and ovarian cancer. According to the US National Cancer Institute, during her life time a woman has a 60% chance of developing breast cancer and 15-40% chance of developing ovarian cancer if she inherits a harmful BRCA mutation. These risks are 5 times and over 10 times more likely than for women without the mutation, respectively.

***Orphan Designation***

*European Union*

During May 2008, we received designation from the EMA for sapacitabine as an orphan medicine in two separate indications: AML and MDS. The EMA's Committee for Orphan Medicinal Products, or COMP, adopted a positive opinion on our 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, EMA scientific advice on protocol development, direct access to the centralized procedure for review of marketing authorizations, EMA 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.

Table of Contents

*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, CDK5, 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 2 clinical trial in patients with NSCLC*

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.



Table of Contents

*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 nasopharyngeal cancer, or 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 OS, 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, which is dependent on clinical data from the lead-in phase and available resources to fund 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.

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 highly-selective, orally-available, 2nd generation inhibitor of CDK -2, -5 and -9; enzyme complexes that play pivotal roles in cancer cell growth, metastatic spread and DNA damage repair. CYC065 causes apoptotic cell death of cancer cells at sub-micromolar and antitumor efficacy has been achieved in vivo with once a day oral dosing at well tolerated doses. CYC065 has been shown to target key components of leukemogenic and survival pathways in acute leukemias, including the MCL1 anti-apoptotic protein, and also transcription, driven by the rearranged mixed lineage leukemia gene. Strong preclinical data supports expansion into solid tumor indications which overexpress cyclin E or CDK5 such as trastuzumab resistant breast cancer and metastatic pancreatic cancer. CYC065 is currently in IND-directed preclinical development.

In addition CYC065 was shown to have preclinical efficacy in proliferative kidney disease models (Cyclacel data on file). 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.

***Plk inhibitors***

In our Plk inhibitor program, CYC140, 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. At the 2012 Annual Meeting of the AACR we reported on one of these compounds selected for further preclinical development. In a panel of esophageal cancer cell lines, sensitivity to CYC140 correlated with p53 status. Esophageal cell lines lacking functional p53 showed the greatest sensitivity to Compound 4. Short drug exposure times demonstrated differential sensitivity between cancerous esophageal cells versus control, outlining the potential broad therapeutic index for Compound 4 in treating esophageal cancers, and in particular those with non-functional p53. Status of p53 could be used as a predictive biomarker in clinical trials to

identify responders. Plk was discovered by Professor David Glover, our Chief Scientist.

Table of Contents

*Aurora kinase inhibitors*

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. At the Annual Meeting of the AACR 2012 we reported that collaborators testing of the activity of CYC3, our novel Aurora Kinase A specific inhibitor, in pancreatic cancer cell lines. They reported that CYC3 suppresses pancreatic cancer cell growth, inducing mitotic arrest and apoptosis. CYC3 was also shown to act synergistically against pancreatic cancer cell lines in combination with paclitaxel at a 10-fold lower dose resulting in comparable anti-proliferative activity to standard paclitaxel dosing. As myelosuppression is associated with paclitaxel administration, the CYC3/low-dose paclitaxel combination was compared with high-dose paclitaxel in an in vitro granulocyte and macrophage assay in which the CYC3/low-dose paclitaxel combination displayed less myelotoxicity. They reported that the combination merits further investigation and has the potential for improved therapeutic index in vivo. In June 2007, we initiated and completed 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. Further work on this program will be undertaken if we have a sufficient level of resources available to direct to the program. We have retained worldwide rights to commercialize CYC116 and our other Aurora kinase inhibitors.

**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.

**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.

Table of Contents

**THE OFFERING**

**Common stock covered hereby** 624,445 shares of common stock, consisting of :

- 29,932 shares of common stock; and
- up to 594,513 shares of common stock issuable upon exercise of outstanding warrants

**Common stock outstanding as of April 12, 2013** 10,831,779 shares

**Use of proceeds** We will not receive any proceeds from the sale or other disposition of common stock by the selling stockholders. In the event that the outstanding Warrants are exercised for cash, we may receive up to a total of approximately \$8.0 million in proceeds. However, we cannot predict the timing or the amount of the exercise of these securities. 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 exercise of the Warrants by their holders. 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 11.

**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.

Table of Contents

**RISK FACTORS**

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

*We have grouped risks into several categories in order of their potential impact on our results of operations, financial condition, and cash flows.*

**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 AML.*

On September 13, 2010, and as amended on October 11, 2011, 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 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. In January 2011, we opened enrollment in the lead-in portion of the SEAMLESS trial and in October 2011, we opened enrollment in the randomized portion of the 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.

**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.**

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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.

Table of Contents

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 and we cannot be certain that we will be able to raise sufficient funds to complete the development and commercialize any of our product candidates currently in clinical development, should they succeed.***

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 more years 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 IRB and other regulatory approvals to commence a clinical trial;
  
- slower than anticipated rates of patient recruitment and enrollment, or not reaching the targeted number of patients because of competition for patients from other trials, or if there is limited or no availability of coverage, reimbursement and adequate payment from health maintenance organizations and other third party payors for the use of agents used in our clinical trials, such as decitabine in SEAMLESS, 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 pharmacodynamics 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.

Table of Contents

***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.

***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.



Table of Contents

***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.

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 a 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.

Table of Contents

***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. With respect to the ALIGN products, we relied on Sinclair to manufacture our commercial products until the agreement with Sinclair was terminated on September 30, 2012. We currently lack the resources or the capacity to manufacture any of our products on a clinical or commercial scale. We anticipate future reliance on a limited number of third party manufacturers until we are able, or decide to, expand our operations to include manufacturing capacities. 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. 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.

***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