Cyclacel Pharmaceuticals, Inc.
Form 424B5
May 15, 2013
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The information contained in this preliminary prospectus supplement is not complete and may be changed. A registration statement relating to these securities has been declared effective by the Securities and Exchange Commission. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities, and we are not soliciting offers to buy these securities in any jurisdiction where the offer or sale is not permitted.

Filed Pursuant to Rule 424(b)(5)
Registration No. 333-187801

Dated May 15, 2013

Prospectus Supplement
(to Prospectus dated April 22, 2013)

Shares of Common Stock

CYCLACEL PHARMACEUTICALS, INC.

We are offering up to shares of our common stock at a negotiated price of $ per share. For a more detailed description of our common stock, see the section entitled Description of the Securities we are Offering beginning on page S-19 of this prospectus supplement.

Our common stock is listed on The NASDAQ Global Market under the symbol CYCC. On May 14, 2013, the last reported sale price of our common stock on The NASDAQ Global Market was $3.71 per share.

Investing in our securities involves a high degree of risk. Please read Risk Factors beginning on page S-12 of this prospectus supplement, page 13 of the accompanying prospectus and the documents incorporated by reference into this prospectus supplement.

	Per Share	Maximum Offering Amount
Price to the public	$	$
Underwriting discounts and commissions	$	$
Proceeds, before expenses, to us	$	$

The underwriters may also purchase up to an additional shares from us at the public offering price, less the underwriting discount, within 30 days from the date of this prospectus supplement to cover overallotments, if any. If the underwriters exercise the option in full, the total discount will be $ and the total net proceeds, before expenses, to us will be $.

The underwriters expect to deliver the shares on or about May , 2013.

You should carefully read this prospectus supplement and the accompanying prospectus, together with the documents we incorporate by reference, before you invest in our securities.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

JMP Securities

Sole Book-Running Manager

Janney Montgomery Scott

Co-Manager

The date of this prospectus supplement is May , 2013.

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You should only rely on the information contained in, or incorporated by reference in, this prospectus supplement and the accompanying prospectus. We and the underwriters have not authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We and the underwriters are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information contained in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein is accurate as of any date other than the dates of the specific information. Our business, financial condition, results of operations and prospectus may have changed since then.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the terms of this offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part, the accompanying prospectus dated April 22, 2013, including the documents incorporated by reference therein, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined.

To the extent there is a conflict between the information contained in this prospectus supplement or any free writing prospectus we may authorize to be delivered to you, on the one hand, and the information contained in the accompanying prospectus or in any document incorporated by reference that was filed with the Securities and Exchange Commission, or SEC, before the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement or such free writing prospectus, as the case may be. If any statement in one of these documents is inconsistent with a statement in another document having a later date, the statement in the document having the later date modifies or supersedes the earlier statement. You should also read and consider the information in the documents to which we refer you in Where You Can Find More Information on page S-21 of this prospectus supplement and any free writing prospectus we may authorize to be delivered to you. The information incorporated by reference is considered to be part of this prospectus supplement, and information that we file later with the SEC will automatically update and supersede this information.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference herein were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

This prospectus supplement, the accompanying prospectus, and the information incorporated herein and therein by reference include trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included or incorporated by reference into this prospectus supplement or the accompanying prospectus are the property of their respective owners.

We are offering to sell, and seeking offers to buy, units only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the accompanying prospectus and the offering of the units in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement and the accompanying prospectus must inform themselves about, and observe any restrictions relating to, the offering of the units and the distribution of this prospectus supplement and the accompanying prospectus outside the United States. This prospectus supplement and the accompanying prospectus do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

The terms Cyclacel, the Company, we and us in this prospectus supplement refer to Cyclacel Pharmaceuticals, Inc. and its subsidiaries, unless the context otherwise requires.

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PROSPECTUS SUPPLEMENT SUMMARY

This summary may not contain all of the information that may be important to you. You should read this prospectus supplement, the accompanying prospectus, the information incorporated by reference in each, and any related free writing prospectus before making an investment decision. You should pay special attention to the Risk Factors section beginning on page S-12 of this prospectus supplement, as well as to any Risk Factor included in the accompanying prospectus and in any document incorporated into this prospectus supplement or the accompanying prospectus by reference, to determine whether an investment in our common stock is appropriate for you.

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
- Solid tumors, including breast cancer, non-small cell lung cancer, or NSCLC, ovarian cancer and pancreatic cancer.

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. Sapacitabine is also being evaluated in a Phase1 study in combination with seliciclib, our second clinical candidate, in patients with solid tumors.

The Company has evaluated seliciclib, an orally-available, highly selective inhibitor of CDK enzymes, in Phase 2 studies in NSCLC and nasopharyngeal cancer, or NPC. The Company will determine the feasibility of pursuing further development and/or partnering this asset and/or indications subject to available resources.

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

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In addition to these development programs, the Company has allocated limited resources to other programs allowing the Company to maintain and build on its core competency in cell cycle biology and related drug discovery, including its polo-like kinase, or PLK, inhibitor program, the Company discovered CYC140, a potent and selective, orally-available, small molecule inhibitor of PLK1, a kinase active during cell division, targeting the mitotic phase of the cell cycle. In the Company s Aurora kinase inhibitor program, CYC116, an internally-discovered, orally-available, small molecule inhibitor of Aurora kinases A and B and Vascular Endothelial Growth Factor Receptor 2, or VEGFR2, has completed a multicenter Phase 1 trial. PLK and Aurora are cancer drug targets discovered by Professor David Glover, the Company s Chief Scientist.

We also have other 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 a 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 cancer cell DNA synthesis through the incorporation of CNDAC into DNA during replication or repair, triggering a beta-elimination reaction and leading to the formation of single-strand breaks, or 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, or DSBs. DSBs can be repaired by the homologous recombination repair (HRR) pathway, or, if unrepaired, result in cancer cell death.

We are currently exploring sapacitabine in both hematological cancers and solid tumors, Over 600 patients have received sapacitabine in Phase 1, 2 and 3 studies.

Hematological Cancers

SEAMLESS randomized Phase 3 pivotal trial in elderly patients with AML

The SEAMLESS study is being conducted under an SPA, or Special Protocol Assessment, agreement that Cyclacel reached with the FDA. The study is evaluating sapacitabine 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 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 the experimental arm, oral sapacitabine is administered in alternating cycles with intravenous decitabine and in control arm intravenous

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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, 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, once 212 events have been observed. In addition, the DSMB will periodically convene to review data for safety 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, were 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 with a range 70-90. Median overall survival was 238 days, or approximately 8 months. The number of patients still alive at three months was 38, or 83%, at six months 30, or 65%, at twelve months 16, or 35%, and at eighteen months 12, or 26%. Sixteen patients, or 35%, survived 1 year or longer. Among 33, or 72%, 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, or 41%, responded with 10 complete responses, or CRs, 4 partial responses, or PRs, and 5 major hematological improvement, or HIs. Median time to response was 2 cycles, i.e., one cycle of decitabine and one cycle of sapacitabine with a range 1-10. Twenty-seven patients, or 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 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 as a single agent 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 HI 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 which produces a better one year survival rate in the event that all three dosing schedules are active.

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, or 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: 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. 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

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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 CRs in 25% of patients. The median overall survival of patients from all groups who achieved CR was 525 days with a 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 trial in older patients with MDS as a second-line treatment

In addition to our studies in AML, 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 which 52 were classified as intermediate-2 and 11 as high-risk by the International Prognostic Scoring System or IPSS, at study entry. All patients received sapacitabine every 4 weeks on one of 3 dosing schedules: G. 200 mg twice daily for 7 days; H. 300 mg once daily for 7 days; or I. 100 mg once daily for 5 days per week for 2 weeks. 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, or also lenalidomide. Secondary objectives are to assess the number of patients who have achieved CR or CRp, PR, HI 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 interim data from this ongoing Phase 2 trial. Median overall survival to date for all 63 patients was 252 days or approximately 8 months. Median overall survival for each arm was 291 days or approximately 10 months for Arm G, 274 days or approximately 9 months for Arm H, and 227 days or approximately 8 months for Arm I. 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. 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.

In April 2013, we reported updated median overall survival data from the above ongoing, multicenter, Phase 2 randomized trial. The updated median overall survival for all three arms was 259 days or approximately 9 months. The median overall survival for each arm was 291 days or approximately 10 months for Arm G, 290 days or approximately 10 months for Arm H, and 227 days or approximately 8 months for Arm I. Median number of cycles was 3. Approximately 43% of patients received 4 or more cycles. Median follow-up is 524 days and 13 patients are still alive.

Median survival for patients with intermediate-2 or high-risk disease, as defined by IPSS, is 4.3 to 5.6 months as reported in the 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 trial in patients with NSCLC

We are evaluating sapacitabine as a single agent 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,

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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 or day 1-7 and seliciclib twice daily for 3 days or 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.

Among 19 patients treated at the MTD, 3 partial responses or 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 genome. 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.

In April 2013, at the 104th Annual Meeting of the American Association of Cancer Research, or AACR, we reported updated data from this ongoing Phase 1 trial. To date, 38 patients with incurable solid tumors and adequate organ function have been enrolled in the Phase 1 study, 16 of them found to be BRCA mutation carriers. Four patients with BRCA-deficient pancreatic, breast or ovarian cancers had confirmed partial responses to the drug combination. Based on available follow-up, three patients experienced durable partial responses, with the longest lasting more than 78 weeks. Researchers observed stable disease of 12 weeks or more in eight additional patients, including two patients with ovarian and breast cancers who

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carried BRCA mutations and whose stable disease lasted 64 weeks and 21 weeks, respectively. The maximum tolerated doses were 50 mg sapacitabine twice daily and 1,200 mg seliciclib twice daily. Dose-limiting toxicities included reversible transaminase elevations and neutropenia. Adverse events were mild to moderate in intensity. Results of skin biopsies after treatment showed a 2.3-fold increase in DNA damage induced by sapacitabine, as measured by gamma-H2AX immunohistochemistry. Additional DNA damage occurred after treatment with seliciclib with a 0.58-fold further increase in gamma-H2AX staining.

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 both 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 sapacitabine for 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 US government to defray costs of clinical trial expenses, tax credits for clinical research expenses and a potential waiver of the FDA s application user fee. Orphan status is granted by the FDA to promote the development of new drug therapies for the treatment of diseases that affect fewer than 200,000 individuals in the United States.

Seliciclib

Although our current clinical development priorities are focused on sapacitabine only, our second drug candidate, seliciclib, is a novel, first-in-class, orally-available, CDK inhibitor. Seliciclib selectively targets CDK2, CDK7 and CDK9, enzymes 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 is more active against NSCLC cells with K-Ras or N-Ras mutations than those with wild type Ras and overcomes resistance to letrozole or 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

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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 trials in patients with NSCLC and other cancers

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, of 48 versus 53 days respectively, but an increase in median overall survival, or OS, was observed favoring the seliciclib arm over the placebo arm of 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, or 28%, were randomized, 27 on seliciclib and 26 on placebo. Forty-five out of 53 randomized patients, or 85%, received 3 or more prior therapies and 45 out of 53 randomized patients, or 85%, previously received at least one EGFR inhibitor drug, of which 22 were 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.

Published pre-clinical work indicated that K-Ras mutational status, cyclin D1 and cyclin E1 protein levels correlated strongly with tumor sensitivity after exposure to seliciclib. In order to explore a 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 had given informed consent, results of the retrospective analysis were insufficient to allow meaningful correlation. A new prospectively designed study is required to test the hypothesis that certain biomarkers can predict therapeutic effect of seliciclib in patients with advanced stage NSCLC.

Phase 2 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

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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, second generation inhibitor of CDK2, CDK5 and CDK9; 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 levels 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, or MLL, 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 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, 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 CYC140, a PLK1 inhibitor selected for further preclinical development. In a cell line panel of esophageal cancer CYC140 activity correlated with p53 status, as the greatest sensitivity to CYC140 was observed in cell lines lacking functional p53. Short drug exposure times demonstrated differential sensitivity between cancerous esophageal cells versus control, outlining the potential broad therapeutic index for CYC140 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.

Aurora kinase inhibitors

Aurora kinases, or AK, are a family of serine/threonine protein kinases discovered by Professor David Glover, our Chief Scientist. AK are only expressed in actively dividing cells and are crucial for cell division, or mitosis. AK proteins are over-expressed in many cancer types and 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 2012 Annual Meeting of the AACR we reported that CYC3, our novel AK A specific inhibitor, suppressed pancreatic cancer cell growth, inducing mitotic arrest and apoptosis. CYC3 acted synergistically against pancreatic cancer cell lines in combination with paclitaxel at a 10-fold

lower dose to standard paclitaxel dosing resulting in comparable anti-proliferative activity. CYC3/low-dose paclitaxel combination displayed less myelotoxicity to high-dose paclitaxel suggesting that the combination merits further investigation and may have improved therapeutic index *in vivo*. We previously completed a multicenter Phase 1 pharmacologic clinical trial of CYC116, our novel AK A and B and VEGFR2 inhibitor, in patients with advanced solid tumors.

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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.

Possible Director Participation

Certain of our executive and non-executive directors have indicated an interest in purchasing up to an aggregate of not more than $1 million of shares of common stock in this offering at the public offering price. Because this indication of interest is not a binding agreement or commitment to purchase, they may elect not to purchase any shares in this offering, or the underwriters may elect not to sell any shares in this offering to them.

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. Our Internet address is www.cyclacel.com. The information on our website is not part of this prospectus supplement.

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THE OFFERING

Securities offered by us	shares of our common stock.
Offering price per share	$
Underwriters option to purchase additional shares	shares of common stock.
Common stock outstanding immediately after this offering(1)	shares of common stock.
Use of proceeds	We intend to use the net proceeds from the sale of our common stock offered hereby for funding our SEAMLESS pivotal Phase 3 trial of our leading drug, Sapacitabine, and general corporate purposes.
Risk factors	You should read the description of risks set in the Risk Factors sections on Page S-12 of this prospectus supplement and page 13 of the accompanying prospectus or otherwise incorporated by reference in this prospectus supplement and the accompany prospectus for a discussion of material risks that prospective purchasers of shares of our common stock should consider.
NASDAQ Symbol	CYCC

(1) Based on 10,881,780 shares of our common stock outstanding as of March 31, 2013 and assumes that all of the shares offered hereby are sold. Except as otherwise indicated, all information in the prospectus supplement assumes no exercise by the underwriters of their overallotment option.

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RISK FACTORS

Investing in our securities involves a high degree of risk. Before purchasing our securities, you should carefully consider the following risk factors and those set forth in the accompanying prospectus, together with those risk factors set forth in our most recent Annual Report on Form 10-K for the year ended December 31, 2012, and in our Quarterly Report on Form 10-Q for the three month period ended March 31, 2013, which are incorporated by reference into this prospectus supplement. You should also carefully consider all of the other information in this prospectus supplement, the accompanying prospectus, or incorporated by reference into this prospectus supplement and the accompanying prospectus. Any of these risks could have a material adverse impact on our business, prospects, results of operations and financial condition and could therefore have a negative effect on the trading price of our common stock and you might lose all or part of your investment in our securities. Additionally, risks not currently known to us or that we now deem immaterial may also harm us and negatively affect your investment. The following risks are presented as of the date of this prospectus supplement and we expect that these will be updated from time to time in our periodic and current reports filed with the SEC, which will be incorporated herein by reference. Please refer to these subsequent reports for additional information relating to the risks associated with investing in our common stock. See Where You Can Find More Information and Incorporation of Certain Information by Reference.

Risks Related to This Offering

Management will have broad discretion as to the use of the proceeds from this offering, and we may not use the proceeds effectively.

Our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. Our failure to apply these funds effectively could have a material adverse effect on our business and cause the price of our common stock to decline.

You will experience immediate and substantial dilution in the net tangible book value per share of the common stock you purchase.

Since the price per share of our common stock being offered is substantially higher than the net tangible book value per share of our common stock, you will suffer immediate dilution in the net tangible book value of the common stock you purchase in this offering. After giving effect to the sale of shares of our common stock in this offering at the offering price of $ per share, and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, you will experience immediate dilution of $ per share, representing the difference between our as adjusted net tangible book value per share as of March 31, 2013 after giving effect to this offering and the offering price. See the section entitled Dilution below for a more detailed discussion of the dilution you will incur if you purchase the common stock in this offering.

You may experience future dilution as a result of future equity offerings.

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock. We cannot assure you that we will be able to sell shares or other securities in any other offering at a price

per share that is equal to or greater than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock or other securities convertible into or exchangeable

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for our common stock in future transactions may be higher or lower than the price per share in this offering.

SPECIAL NOTE REGARDING FORWARD-LOOKING INFORMATION

Certain statements contained or incorporated by reference into this prospectus supplement, the accompanying prospectus and any related free writing prospectus constitute forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Exchange Act, including statements, other than statements of historical facts, included or incorporated in this prospectus supplement, the accompanying prospectus and any related free writing prospectus regarding our strategy, anticipated agreements with marketing partners, progress and timing of research and product development results, anticipated clinical trial timelines or results, projected regulatory timelines, future operations, financial position, future revenues, projected costs, prospects, plans, and objectives of management. The words may, will, should, would, expect, intend, plan, anticipate, believe, estimate, predict, potential, continue, or a terms or similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We cannot guarantee that we actually will achieve the plans, intentions or expectations disclosed in our forward-looking statements and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. In evaluating such forward-looking statements, you should specifically consider various factors, including the risks outlined under the heading Risk Factors contained in any related free writing prospectus and in this prospectus supplement and the accompanying prospectus, and in our most recent annual report on Form 10-K and any subsequent filings with the SEC. The discussion of risks and uncertainties set forth in those filings is not necessarily a complete or exhaustive list of all risks facing the Company at any particular point in time. We operate in a highly competitive, highly regulated and rapidly changing environment, and our business is in a state of evolution. Therefore, it is likely that new risks will emerge, and that the nature and elements of existing risks will change, over time. It is not possible for management to predict all such risk factors or changes therein, or to assess either the impact of all such risk factors on our business or the extent to which any individual risk factor, combination of factors, or new or altered factors, may cause results to differ materially from those contained in any forward-looking statement. Also, these forward-looking statements represent our estimates and assumptions only as of the date such forward-looking statements are made. We are not under any obligation, and we expressly disclaim any obligation, to update or alter any forward-looking statements, whether as a result of new information, future events or otherwise. All subsequent forward-looking statements attributable to Cyclacel or to any person acting on its behalf are expressly qualified in their entirety by the cautionary statements contained or referred to in this section.

We cannot assure you that the forward-looking statements in this prospectus supplement, the accompanying prospectus, any related free writing prospectus and the documents incorporated by reference herein and therein will prove to be accurate. In addition, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, if at all. We may not update these forward-looking statements, even though our situation may change in the future.

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USE OF PROCEEDS

We estimate that the net proceeds from this offering will be approximately $ million, or approximately $ if the underwriters exercise in full their option to purchase up to additional shares of common stock, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. We intend to use the net proceeds of this offering for funding our SEAMLESS pivotal Phase 3 trial of our leading drug, sapacitabine, and general corporate purposes. Pending use of the net proceeds, we intend to invest these net proceeds in interest bearing investment grade securities.

DILUTION

Our net tangible book value as of March 31, 2013, was approximately $10,234,000, or $0.94 per share of common stock. Net tangible book value per share is calculated by subtracting our total liabilities from our total tangible assets, which is total assets less intangible assets, and dividing this amount by the number of shares of common stock outstanding. After giving effect to the sale by us of the shares of common stock offered in this offering, at an offering price of $ per share and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, our net tangible book value as of March 31, 2013, would have been approximately $ million, or $ per share of common stock. This represents an immediate increase in net tangible book value of $ per share to our existing stockholders and an immediate and substantial dilution of $ per share to new investors. The following table illustrates this per share dilution:

Offering price per share		$
Net tangible book value per share as of March 31, 2013	$ 0.94	
Increase per share after the offering	$	
Net tangible book value per share after this offering		$
Dilution per share to new investors		$

If the underwriters exercise in full their option to purchase up to additional shares of common stock, the as adjusted net tangible book value after this offering would be $ per share, representing an increase in net tangible book value of $ per share to existing stockholders and immediate dilution of $ per share to investors purchasing our common stock in this offering at the public offering price. The foregoing table does not take into account further dilution to new investors that could occur upon the exercise of outstanding options and warrants having a per share exercise price less than the per share offering price to the public in this offering. As of March 31, 2013, there were 10,881,780 shares of common stock outstanding, which does not include the following (each as of March 31, 2013):

- 463,023 shares of common stock issuable upon the exercise of outstanding options at a weighted-average exercise price of $26.61 per share;

- 220,595 shares of contingently issuable shares of common stock and common stock purchase warrants associated with the economic rights pursuant to the Purchase Agreement dated March 22, 2012 between the Company and certain investors signatory thereto, which securities will not be issued given the termination of the economic rights;

- 124,474 shares of common stock issuable upon restricted common stock units;

- 757,320 shares of common stock available for issuance under our 2006 Equity Incentive Plan;

- 1,973,427 shares of common stock issuable upon the exercise of outstanding warrants at a weighted-average exercise price of $22.96 per share; and

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- 25,573 shares of common stock, subject to adjustment, that are issuable upon the conversion of 420,682 shares of convertible preferred stock that are issued and outstanding.

Except as otherwise indicated, all information in the prospectus supplement assumes no exercise by the underwriters of their overallotment option.

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UNDERWRITING

We and the underwriters for the offering named below have entered into an underwriting agreement with respect to the shares of common stock being offered. Subject to the terms and conditions of the underwriting agreement, each underwriter has severally agreed to purchase from us the number of shares of common stock set forth opposite its name below. JMP Securities LLC is the representative of the underwriters.

Underwriter	Number of Shares of Common Stock
JMP Securities LLC	
Janney Montgomery Scott LLC	
Total	

The underwriters are offering the shares of common stock subject to each underwriter s acceptance of the shares of common stock from us and subject to prior sale. The underwriting agreement provides that the obligation of each underwriter to pay for and accept delivery of the shares of common stock offered by this prospectus supplement and the related prospectus is subject to the approval of certain legal matters by its counsel and to certain other conditions. Each underwriter is obligated to take and pay for all of the shares of common stock if any such shares are taken.

Over-Allotment Option

We have granted the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase up to an aggregate of additional shares of common stock to cover over-allotments, if any, at the public offering price set forth on the cover page of this prospectus supplement, less underwriting discounts and commissions. The underwriters may exercise this option solely for the purpose of covering over-allotments, if any, made in connection with the offering of the shares of common stock offered by this prospectus supplement and the accompanying prospectus.

Commission and Expenses

The underwriters have advised us that they propose to offer the shares of common stock to the public at the initial public offering prices set forth on the cover page of this prospectus supplement and to certain dealers at that price less a concession not in excess of $ per share of common stock. The underwriters may allow, and certain dealers may reallow, a discount from the concession not in excess of $ per share of common stock to certain brokers and dealers. After this offering, the initial public offering price, concession and reallowance to dealers may be changed by the underwriters. No such change shall change the amount of proceeds to be received by us as set forth on the cover page of this prospectus supplement. The shares of common stock are offered by the underwriters subject to various conditions as stated herein, including receipt and acceptance by it and its right to reject any order in whole or in part. The underwriters have informed us that they do not intend to confirm sales to any accounts over which they exercise discretionary authority.

The following table shows the underwriting discounts and commissions payable to the underwriters by us in connection with this offering.

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	Per Share of Common Stock	Total Without Exercise of Over-Allotment Option	Total with Full Exercise of Over-Allotment Option
Public offering price	$	$	$
Underwriting discounts and commissions payable by us	$	$	$

We estimate that expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately $. We have agreed to reimburse the underwriters for certain out-of-pocket expenses not to exceed $120,000 for all expenses, including attorneys fees and expenses actually incurred.

Indemnification

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act of 1933, as amended, or the Securities Act, and liabilities arising from breaches of representations and warranties contained in the underwriting agreement, or to contribute to payments that the underwriters may be required to make in respect of those liabilities.

Lock-up Agreements

We, our officers and directors have agreed, subject to limited exceptions, for a period of 90 days after the date of the underwriting agreement, not to offer, sell, contract to sell, pledge, grant any option to purchase or otherwise dispose of, directly or indirectly any shares of common stock or any securities convertible into or exchangeable for our common stock either owned as of the date of the underwriting agreement or thereafter acquired without the prior written consent of JMP Securities LLC. This 90-day period may be extended if (1) during the last 17 days of the 90-day period, we issue an earnings release or material news or a material event regarding us occurs or (2) prior to the expiration of the 90-day period, we announce that we will release earnings results during the 16-day period beginning on the last day of the 90-day period, then the period of such extension will be 18 days, beginning on the issuance of the earnings release or the occurrence of the material news or material event. If after any announcement described in clause (2) of the preceding sentence, we announce that we will not release earnings results during the 16-day period, the lock-up period shall expire at the later of the expiration of the 90-day period and the end of any extension of such period made pursuant to clause (1) of the preceding sentence. JMP Securities LLC may, in its sole discretion and at any time or from time to time before the termination of the lock-up period, without notice, release all or any portion of the securities subject to lock-up agreements.

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Price Stabilization, Short Positions and Penalty Bids

In connection with the offering the underwriters may engage in stabilizing transactions, over-allotment transactions and syndicate covering transactions in accordance with Regulation M under the Exchange Act:

- Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum.

- Over-allotment involves sales by the underwriters of shares in excess of the number of shares the underwriters are obligated to purchase, which creates a syndicate short position. The short position may be either a covered short position or a naked short position. In a covered short position, the number of shares over-allotted by the underwriters is not greater than the number of shares that they may purchase in the over-allotment option. In a naked short position, the number of shares involved is greater than the number of shares in the over-allotment option. The underwriters may close out any covered short position by either exercising their over-allotment option and/or purchasing shares in the open market.

- Syndicate covering transactions involve purchases of shares of the common stock in the open market after the distribution has been completed in order to cover syndicate short positions. In determining the source of shares to close out the short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which it may purchase shares through the over-allotment option. If the underwriters sell more shares than could be covered by the over-allotment option, a naked short position, the position can only be closed out by buying shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there could be downward pressure on the price of the shares in the open market after pricing that could adversely affect investors who purchase in the offering.

Electronic Distribution

This prospectus supplement and the related prospectus in electronic format may be made available on websites or through other online services maintained by the underwriters, or by their affiliates. Other than this prospectus supplement and the related prospectus in electronic format, the information on any underwriter s website and any information contained in any other website maintained by any underwriter is not part of this prospectus supplement, the related prospectus or the registration statement of which this prospectus supplement and the related prospectus forms a part, has not been approved and/or endorsed by us or the underwriters in their capacity as underwriters, and should not be relied upon by investors.

Other

The underwriters and/or their affiliates have provided, and may in the future provide, various investment banking and other financial services for us for which services they has received and, may in the future receive, customary fees.

Transfer Agent

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC. Its address is 59 Maiden Lane, Plaza Level, New York, NY 10038, and their telephone number is (800) 937-5449.

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DESCRIPTION OF THE SECURITIES WE ARE OFFERING

In this offering, we are offering a maximum of shares of common stock. The underwriters may also purchase up to an additional shares from us at the public offering price, less the underwriting discount, within 30 days from the date of this prospectus supplement to cover overallotments, if any.

Common Stock

We are authorized to issue 100,000,000 shares of common stock, $0.001 par value. As of March 31, 2013, 10,881,780 shares of common stock were issued and outstanding. The following descriptions of our common stock and provisions of our amended and restated certificate of incorporation and amended and restated by-laws are only summaries, and we encourage you to review complete copies of these documents, which have been filed as exhibits to our periodic reports with the SEC.

Dividends, Voting Rights and Liquidation

Holders of common stock are entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders, and do not have cumulative voting rights. Subject to preferences that may be applicable to any outstanding shares of preferred stock, holders of common stock are entitled to receive ratably such dividends, if any, as may be declared from time to time by our board of directors out of funds legally available for dividend payments. All outstanding shares of common stock are fully paid and non-assessable, and the shares of common stock to be issued upon completion of this offering will be fully paid and non-assessable. The holders of common stock have no preferences or rights of conversion, exchange, pre-emption or other subscription rights. There are no redemption or sinking fund provisions applicable to the common stock. In the event of any liquidation, dissolution or winding-up of our affairs, holders of common stock will be entitled to share ratably in our assets that are remaining after payment or provision for payment of all of our debts and obligations and after liquidation payments to holders of outstanding shares of preferred stock, if any.

Delaware Law and Certain Charter and By-law Provisions

The provisions of (1) Delaware law, (2) our amended and restated certificate of incorporation, and (3) our amended and restated bylaws discussed below could discourage or make it more difficult to accomplish a proxy contest or other change in our management or the acquisition of control by a holder of a substantial amount of our voting stock. It is possible that these provisions could make it more difficult to accomplish, or could deter, transactions that stockholders may otherwise consider to be in their best interests or in our best interests. These provisions are intended to enhance the likelihood of continuity and stability in the composition of our board of directors and in the policies formulated by the board of directors and to discourage certain types of transactions that may involve an actual or threatened change of control of us. These provisions are designed to reduce our vulnerability to an unsolicited acquisition proposal. The provisions also are intended to discourage certain tactics that may be used in proxy fights. Such provisions also may have the effect of preventing changes in our management.

Delaware Statutory Business Combinations Provision. We are subject to the anti-takeover provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is, or the transaction in which the person became an interested stockholder was, approved in a prescribed manner or another prescribed exception applies. For purposes of Section 203, a business combination is defined broadly to include a merger, asset sale or other transaction resulting in a financial benefit to the interested stockholder, and, subject to certain exceptions, an interested stockholder is a person who, together with his or her affiliates and associates, owns (or within three years prior, did own) 15% or more of the corporation s voting stock.

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Classified Board of Directors. Our amended and restated certificate of incorporation and amended and restated bylaws provide that our board of directors is divided into three classes, each serving staggered three-year terms ending at the annual meeting of our stockholders. All directors elected to our classified board of directors will serve until the election and qualification of their respective successors or their earlier resignation or removal. The board of directors is authorized to create new directorships and to fill such positions so created and is permitted to specify the class to which any such new position is assigned. The person filling such position would serve for the term applicable to that class. The board of directors (or its remaining members, even if less than a quorum) is also empowered to fill vacancies on the board of directors occurring for any reason for the remainder of the term of the class of directors in which the vacancy occurred. These provisions are likely to increase the time required for stockholders to change the composition of the board of directors. For example, in general, at least two annual meetings will be necessary for stockholders to effect a change in a majority of the members of the board of directors.

Advance Notice Provisions for Stockholder Proposals and Stockholder Nominations of Directors. Our amended and restated bylaws provide that, for nominations to the board of directors or for other business to be properly brought by a stockholder before a meeting of stockholders, the stockholder must first have given timely notice of the proposal in writing to our Secretary. For an annual meeting, a stockholder s notice generally must be delivered not less than 90 days nor more than 120 days prior to the anniversary of the mailing date of the proxy statement for the previous year s annual meeting. Detailed requirements as to the form of the notice and information required in the notice are specified in the amended and restated bylaws. If it is determined that business was not properly brought before a meeting in accordance with our bylaw provisions, such business will not be conducted at the meeting.

Special Meetings of Stockholders. Special meetings of the stockholders may be called only by our board of directors pursuant to a resolution adopted by a majority of the total number of directors.

No Stockholder Action by Written Consent. Our amended and restated certificate of incorporation and amended and restated bylaws do not permit our stockholders to act by written consent. As a result, any action to be effected by our stockholders must be effected at a duly called annual or special meeting of the stockholders.

Super-Majority Stockholder Vote Required for Certain Actions. The Delaware General Corporation Law provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation s certificate of incorporation or bylaws, unless the corporation s certificate of incorporation or bylaws, as the case may be, requires a greater percentage. Our amended and restated certificate of incorporation requires the affirmative vote of the holders of at least 66 2/3% of our outstanding voting stock to amend or repeal any of the provisions inconsistent with the provisions discussed in the section of this prospectus entitled Classified Board of Directors . This 66 2/3% stockholder vote would be in addition to any separate class vote that might in the future be required pursuant to the terms of any preferred stock that might then be outstanding. In addition, a 66 2/3% vote is also required for any amendment to, or repeal of, our amended and restated bylaws by the stockholders. Our amended and restated bylaws may be amended or repealed by a simple majority vote of the board of directors.

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LEGAL MATTERS

The validity of the securities offered hereby will be passed upon for us by Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., New York, New York. Goodwin Procter LLP, New York, New York, is representing the underwriters in this offering.

EXPERTS

The consolidated financial statements of Cyclacel Pharmaceuticals, Inc. for the year ended December 31, 2010 and the period from August 13, 1996 (inception) to December 31, 2010, appearing in Cyclacel Pharmaceuticals, Inc. s Annual Report on Form 10-K for the year ended December 31, 2012, have been audited by Ernst & Young LLP (UK), independent registered public accounting firm, as set forth in its report thereon, included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

The consolidated financial statements of Cyclacel Pharmaceuticals, Inc. at December 31, 2012, and for each of the two years in the period ended December 31, 2012 and for the period from August 13, 1996 (inception) to December 31, 2012 incorporated by reference in this prospectus have been audited by Ernst & Young LLP (US), independent registered public accounting firm, as set forth in their report thereon incorporated by reference elsewhere herein which, as to the period from August 13, 1996 (inception) to December 31, 2012, are based in part on the report of Ernst & Young LLP (UK), independent registered public accounting firm. The financial statements referred to above are included in reliance upon such reports given on the authority of such firms as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-3 (File No. 333-187801), of which this prospectus supplement and the accompanying prospectus are a part, under the Securities Act, to register the shares of common stock offered by this prospectus supplement. However, this prospectus supplement and the accompanying prospectus do not contain all of the information contained in the registration statement and the exhibits and schedules to the registration statement. We encourage you to carefully read the registration statement and the exhibits and schedules to the registration statement.

As a public company, we are required to file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy any of our materials on file with the SEC at the SEC s Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Our filings are available to the public over the Internet at the SEC s website at http://www.sec.gov. Please call the SEC at 1-800-SEC-0330 for further information on the Public Reference Room.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

In this document, we incorporate by reference certain information we file with the SEC, which means that we can disclose important information to you by referring to that information. The information incorporated by reference is considered to be a part of this prospectus supplement. Any statement contained in a document incorporated by reference herein shall be deemed to be modified or superseded for all purposes to the extent that a statement contained in this prospectus supplement or in any other subsequently filed document that is also incorporated or deemed to be incorporated by reference, modifies or supersedes such statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus supplement. We incorporate by reference the documents listed below (other than any portions thereof that are not deemed filed with the SEC):

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- Our Annual Report on Form 10-K for the year ended December 31, 2012 filed on April 1, 2013;

- Our Current Reports on Form 8-K filed on January 17, 2013, February 1, 2013, March 13, 2013, March 28, 2013, April 4, 2013 and April 8, 2013;

- Our definitive Proxy Statement relating to our 2013 annual meeting of stockholders filed on April 3, 2013;

- Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2013 filed on May 13, 2013;

- The description of our common stock contained in our Registration Statement on Form 8-A, filed on March 8, 2004 (File No. 000-50626), which incorporates by reference the description of the shares of our common stock contained in our Registration Statement on Form S-1 (File No. 333-109653) filed on December 22, 2003 and declared effective by the SEC on March 17, 2004, and any amendment or reports filed with the SEC for purposes of updating such description; and

- The description of our preferred stock contained in our Registration Statement on Form 8-A, filed on October 27, 2004 (File No. 000-50626), which incorporates by reference the description of the shares of our preferred stock contained in our Registration Statement on Form S-1 (File No. 333-119585) filed on October 7, 2004 and declared effective by the SEC on November 1, 2004, and any amendment or reports filed with the SEC for purposes of updating such description

All reports and other documents subsequently filed by us pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act (other than Current Reports on Form 8-K furnished under Item 2.02 or Item 7.01, including any financial statements or other exhibits relating thereto furnished pursuant to Item 9.01 of Form 8-K unless we otherwise state therein) after the date of this prospectus supplement shall be deemed to be incorporated by reference in this prospectus supplement and to be part hereof from the date of filing of such reports and other documents.

We hereby undertake to provide without charge to each person, including any beneficial owner, to whom a copy of this prospectus supplement is delivered, upon written or oral request of any such person, a copy of any and all of the information that has been or may be incorporated by reference in this prospectus supplement, including any exhibits that are specifically incorporated by reference in such documents. Requests for such copies should be directed as follows:

Cyclacel Pharmaceuticals, Inc.
200 Connell Drive, Suite 1500
Berkeley Heights, NJ 07922
(908) 517-7330

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PROSPECTUS

$75,000,000

CYCLACEL PHARMACEUTICALS, INC.

Common Stock
Preferred Stock
Warrants
Debt Securities
Rights
Purchase Contracts
Units

We may, from time to time at prices and on terms to be determined at or prior to the time of one or more offerings, issue up to $75,000,000 of any combination of the securities described in this prospectus, either individually or in units. We may also offer common stock or preferred stock upon conversion of the debt securities, common stock upon conversion of the preferred stock, or common stock, preferred stock or debt securities upon the exercise of warrants, rights or performance of purchase contracts; or any combination of these securities upon the performance of purchase contracts.

This prospectus described the general terms of these securities and the general manner in which these securities will be offered. We will provide you with the specific terms of any offering in one or more supplements to this prospectus. The prospectus supplements will also describe the specific manner in which these securities will be offered and m ay also supplement, update or amend information contained in this document. You should read this prospectus and any prospectus supplement, as well as any documents incorporated by reference into this prospectus or any prospectus supplement, carefully before you invest.

Our common stock is listed on The NASDAQ Global Market under the symbol CYCC, and our preferred stock is listed on the NASDAQ Global Market under the symbol CYCCP. On April 17, 2013, the last reported sale price of our common stock was $5.00 per share, and the last reported sale price of our preferred stock was $8.50. The applicable prospectus supplement will contain information, where applicable, as to any other listing, if any, on The NASDAQ Global Market or any securities market or other securities exchange of the securities covered by the prospectus supplement. Prospective purchasers of our securities are urged to obtain current information as to the market prices of our securities, where applicable.

Investing in our securities involves a high degree of risk. Before deciding whether to invest in our securities, you should consider carefully the risks that we have described on page 13 of this prospectus under the caption Risk Factors. We may include specific risk factors in supplements to this prospectus under the caption Risk Factors. This prospectus may not be used by us to offer or sell our securities unless accompanied by a prospectus supplement.

Our securities may be sold directly by us to investors, through agents designated from time to time or to or through agents, underwriters or dealers. For additional information on the methods of sale, you should refer to the section entitled Plan of Distribution in this prospectus and in the applicable prospectus supplement. If any agents, underwriters or agents are involved in the sale of our securities with respect to which this prospectus is being delivered, the names of such underwriters or agents and any applicable fees, commissions or discounts and over-allotment options will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds that we expect to receive from such sale will also be set forth in a prospectus supplement.

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

The date of this prospectus is April 22, 2013.

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You should read this prospectus and the documents incorporated by reference carefully before you invest. Such documents contain important information you should consider when making your investment decision. See Incorporation of Documents by Reference on page 51. 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.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, utilizing a shelf registration process. Under this shelf registration process, we may offer shares of our common stock, preferred stock, warrants to purchase common stock, and/or debt securities, either individually or in units, in one or more offerings, with a total value of up to $75,000,000. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will contain specific information about the terms of that offering.

This prospectus does not contain all of the information included in the registration statement. For a more complete understanding of the offering of the securities, you should refer to the registration statement, including its exhibits. The prospectus supplement may also add, update or change information contained or incorporated by reference in this prospectus. However, no prospectus supplement will fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness. This prospectus, together with the applicable prospectus supplements and the documents incorporated by reference into this prospectus, includes all material information relating to the offering of securities under this prospectus. You should carefully read this prospectus, the applicable prospectus supplement, the information and documents incorporated herein by reference and the additional information under the heading Where You Can Find More Information before making an investment decision.

You should rely only on the information we have provided or incorporated by reference in this prospectus or any prospectus supplement. We have not authorized anyone to provide you with information different from that contained or incorporated by reference in this prospectus. No dealer, salesperson or other person is authorized to give any information or to represent anything not contained or incorporated by reference in this prospectus. You must not rely on any unauthorized information or representation. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so.

You should assume that the information in this prospectus or any prospectus supplement is accurate only as of the date on the front of the document and that any information we have incorporated herein 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 any sale of a security. To the extent there is a conflict between the information contained in this prospectus and the prospectus supplement, you should rely on the information in the prospectus supplement, provided that if any statement in one of these documents is inconsistent with a statement in another document having a later date for example, a document incorporated by reference in this prospectus or any prospectus supplement the statement in the document having the later date modifies or supersedes the earlier statement.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference in the accompanying prospectus were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

This prospectus may not be used to consummate sales of our securities, unless it is accompanied by a prospectus supplement. To the extent there are inconsistencies between any prospectus supplement,

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this prospectus and any documents incorporated by reference, the document with the most recent date will control.

Unless the context otherwise requires, Cyclacel, the Company, we, us, our and similar terms refer to Cyclacel Pharmaceuticals Inc.

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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 13 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

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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.

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.

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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

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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.

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

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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.

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

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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.

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.

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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

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the hypothesis that these biomarkers can predict therapeutic effect of seliciclib in patients with advanced stage NSCLC.

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 CYC140. Short drug exposure times demonstrated differential sensitivity between cancerous esophageal cells versus control, outlining the potential broad therapeutic index for CYC140 in treating esophageal

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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.

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.

Offerings Under This Prospectus

Under this prospectus, we may offer shares of our common stock and preferred stock, various series of debt securities and/or warrants, rights or purchase contracts to purchase any of such securities, either individually or in units, with a total value of up to $75,000,000, from time to time at prices and on terms to be determined by market conditions at the time of the offering. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

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- designation or classification;
- aggregate principal amount or aggregate offering price;
- maturity, if applicable;
- rates and times of payment of interest or dividends, if any;
- redemption, conversion or sinking fund terms, if any;
- voting or other rights, if any; and
- conversion or exercise prices, if any.

The prospectus supplement also may add, update or change information contained in this prospectus or in documents we have incorporated by reference into this prospectus. However, no prospectus supplement will offer a security that is not registered and described in this prospectus at the time of its effectiveness.

We may sell the securities directly to investors or to or through agents, underwriters or dealers. We, and our agents or underwriters, reserve the right to accept or reject all or part of any proposed purchase of securities. If we offer securities through agents or underwriters, we will include in the applicable prospectus supplement:

- the names of those agents or underwriters;
- applicable fees, discounts and commissions to be paid to them;
- details regarding over-allotment options, if any; and
- the net proceeds to us.

This prospectus may not be used to consummate a sale of any securities unless it is accompanied by a prospectus supplement.

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RISK FACTORS

Investing in our securities involves risk. The prospectus supplement applicable to each offering of our securities will contain a discussion of the risks applicable to an investment in Cyclacel. Prior to making a decision about investing in our securities, you should carefully consider the specific factors set forth below as well as the specific factors discussed under the heading Risk Factors in the applicable prospectus supplement, together with all of the other information contained or incorporated by reference in the prospectus supplement or appearing or incorporated by reference in this prospectus. You should also consider the risks, uncertainties and assumptions discussed under the heading Risk Factors included in our most recent Annual Report on Form 10-K, as revised or supplemented by our subsequent quarterly reports on Form 10-Q or our current reports on Form 8-K, which are on file with the SEC and are incorporated herein by reference, and which may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future. The risks and uncertainties we have described are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our operations.

RATIO OF EARNINGS TO FIXED CHARGES

Any time debt securities are offered pursuant to this prospectus, we will provide a table setting forth our ratio of earnings to fixed charges on a historical basis in the applicable prospectus supplement, if required.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

The SEC encourages companies to disclose forward-looking information so that investors can better understand a company s future prospects and make informed investment decisions. This prospectus contains such forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These statements may be made directly in this prospectus, and they may also be made a part of this prospectus by reference to other documents filed with the SEC which is known as incorporation by reference.

Words such as may, anticipate, estimate, expects, projects, intends, plans, believes and words and terms of similar substance used in with any discussion of future operating or financial performance identify forward-looking statements. All forward-looking statements are management s present expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially from those described in the forward-looking statements. Forward-looking statements might include one or more of the following:

- anticipated results of financing activities;
- anticipated agreements with marketing partners;

- anticipated clinical trial timelines or results;
- anticipated research and product development results;
- projected regulatory timelines;
- descriptions of plans or objectives of management for future operations, products or services;
- forecasts of future economic performance; and
- descriptions or assumptions underlying or relating to any of the above items.

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Please also see the discussion of risks and uncertainties under the heading Risk Factors beginning on page 13.

In light of these assumptions, risks and uncertainties, the results and events discussed in the forward-looking statements contained in this prospectus or in any document incorporated by reference might not occur. Investors are cautioned not to place undue reliance on the forward-looking statements, which speak only as of the date of this prospectus or the date of the document incorporated by reference in this prospectus. We are not under any obligation, and we expressly disclaim any obligation, to update or alter any forward-looking statements, whether as a result of new information, future events or otherwise. All subsequent forward-looking statements attributable to Cyclacel or to any person acting on its behalf are expressly qualified in their entirety by the cautionary statements contained or referred to in this section.

USE OF PROCEEDS

We cannot assure you that we will receive any proceeds in connection with securities offered pursuant to this prospectus. Unless we indicate otherwise in the applicable prospectus supplement, we currently intend to use the net proceeds from this offering for general corporate purposes, including general working capital.

We have not determined the amounts we plan to spend on any of the areas listed above or the timing of these expenditures. As a result, our management will have broad discretion to allocate the net proceeds, if any, we receive in connection with securities offered pursuant to this prospectus for any purpose. Pending application of the net proceeds as described above, we intend to invest the net proceeds of the offering in short-term, investment-grade, interest-bearing securities.

We may set forth additional information on the use of net proceeds from the sale of securities we offer under this prospectus in a prospectus supplement relating to the specific offering.

PLAN OF DISTRIBUTION

We may offer securities under this prospectus from time to time pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods. We may sell the securities (1) through underwriters or dealers, (2) through agents or (3) directly to one or more purchasers, or through a combination of such methods. We may distribute the securities from time to time in one or more transactions at:

- a fixed price or prices, which may be changed from time to time;
- market prices prevailing at the time of sale;
- prices related to the prevailing market prices; or

- negotiated prices.

We may directly solicit offers to purchase the securities being offered by this prospectus. We may also designate agents to solicit offers to purchase the securities from time to time. We will name in a prospectus supplement any underwriter or agent involved in the offer or sale of the securities.

If we utilize a dealer in the sale of the securities being offered by this prospectus, we will sell the securities to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale.

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If we utilize an underwriter in the sale of the securities being offered by this prospectus, we will execute an underwriting agreement with the underwriter at the time of sale, and we will provide the name of any underwriter in the prospectus supplement which the underwriter will use to make resales of the securities to the public. In connection with the sale of the securities, we, or the purchasers of the securities for whom the underwriter may act as agent, may compensate the underwriter in the form of underwriting discounts or commissions. The underwriter may sell the securities to or through dealers, and the underwriter may compensate those dealers in the form of discounts, concessions or commissions.

With respect to underwritten public offerings, negotiated transactions and block trades, we will provide in the applicable prospectus supplement information regarding any compensation we pay to underwriters, dealers or agents in connection with the offering of the securities, and any discounts, concessions or commissions allowed by underwriters to participating dealers. Underwriters, dealers and agents participating in the distribution of the securities may be deemed to be underwriters within the meaning of the Securities Act of 1933, as amended, or the Securities Act, and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions. We may enter into agreements to indemnify underwriters, dealers and agents against civil liabilities, including liabilities under the Securities Act, or to contribute to payments they may be required to make in respect thereof.

If so indicated in the applicable prospectus supplement, we will authorize underwriters or other persons acting as our agents to solicit offers by certain institutions to purchase securities from us pursuant to delayed delivery contracts providing for payment and delivery on the date stated in the prospectus supplement. Each contract will be for an amount not less than, and the aggregate amount of securities sold pursuant to such contracts shall not be less nor more than, the respective amounts stated in the prospectus supplement. Institutions with whom the contracts, when authorized, may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutions, but shall in all cases be subject to our approval. Delayed delivery contracts will not be subject to any conditions except that:

- the purchase by an institution of the securities covered under that contract shall not at the time of delivery be prohibited under the laws of the jurisdiction to which that institution is subject; and

- if the securities are also being sold to underwriters acting as principals for their own account, the underwriters shall have purchased such securities not sold for delayed delivery. The underwriters and other persons acting as our agents will not have any responsibility in respect of the validity or performance of delayed delivery contracts.

Shares of our common stock sold pursuant to the registration statement of which this prospectus is a part will be authorized for quotation and trading on The NASDAQ Global Market. The applicable prospectus supplement will contain information, where applicable, as to any other listing, if any, on The NASDAQ Global Market or any securities market or other securities exchange of the securities covered by the prospectus supplement. We can make no assurance as to the liquidity of or the existence of trading markets for any of the securities.

In order to facilitate the offering of the securities, certain persons participating in the offering may engage in transactions that stabilize, maintain or otherwise affect the price of the securities. This may include over-allotments or short sales of the securities, which involve the sale by persons participating in the offering of more securities than we sold to them. In these circumstances, these persons would cover

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such over-allotments or short positions by making purchases in the open market or by exercising their over-allotment option. In addition, these persons may stabilize or maintain the price of the securities by bidding for or purchasing the applicable security in the open market or by imposing penalty bids, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if the securities sold by them are repurchased in connection with stabilization transactions. The effect of these transactions may be to stabilize or maintain the market price of the securities at a level above that which might otherwise prevail in the open market. These transactions may be discontinued at any time.

In compliance with the guidelines of the Financial Industry Regulatory Authority, Inc., or FINRA, the maximum consideration or discount to be received by any FINRA member or independent broker dealer may not exceed 8% of the aggregate amount of the securities offered pursuant to this prospectus and any applicable prospectus supplement.

The underwriters, dealers and agents may engage in other transactions with us, or perform other services for us, in the ordinary course of their business.

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SECURITIES WE MAY OFFER

The descriptions of the securities contained in this prospectus, together with the applicable prospectus supplements, summarize all the material terms and provisions of the various types of securities that we may offer. We will describe in the applicable prospectus supplement relating to any securities the particular terms of the securities offered by that prospectus supplement. If we indicate in the applicable prospectus supplement, the terms of the securities may differ from the terms we have summarized below. We will also include information in the prospectus supplement, where applicable, about material United States federal income tax considerations relating to the securities, and the securities exchange, if any, on which the securities will be listed.

We may sell from time to time, in one or more offerings:

- common stock;
- preferred stock;
- warrants to purchase common stock;
- debt securities;
- rights;
- purchase contracts; and/or
- units.

This prospectus may not be used to consummate a sale of securities unless it is accompanied by a prospectus supplement.

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DESCRIPTION OF COMMON STOCK

We are authorized to issue 100,000,000 shares of common stock, $0.001 par value per share. As of April 1, 2013, 10,831,779 shares of common stock were issued and outstanding. The following descriptions of our common stock and provisions of our amended and restated certificate of incorporation and amended and restated by-laws are only summaries, and we encourage you to review complete copies of these documents, which have been filed as exhibits to our periodic reports with the SEC.

Transfer Agent

Our transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC.

Listing

Our common stock is listed for quotation on The NASDAQ Global Market under the symbol CYCC.

Dividends, Voting Rights and Liquidation

Holders of common stock are entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders, and do not have cumulative voting rights. Subject to preferences that may be applicable to any outstanding shares of preferred stock, holders of common stock are entitled to receive ratably such dividends, if any, as may be declared from time to time by our board of directors out of funds legally available for dividend payments. All outstanding shares of common stock are fully paid and non-assessable, and the shares of common stock to be issued upon completion of this offering will be fully paid and non-assessable. The holders of common stock have no preferences or rights of conversion, exchange, pre-emption or other subscription rights. There are no redemption or sinking fund provisions applicable to the common stock. In the event of any liquidation, dissolution or winding-up of our affairs, holders of common stock will be entitled to share ratably in our assets that are remaining after payment or provision for payment of all of our debts and obligations and after liquidation payments to holders of outstanding shares of preferred stock, if any.

Delaware Law and Certain Charter and By-law Provisions

The provisions of (1) Delaware law, (2) our amended and restated certificate of incorporation, and (3) our amended and restated bylaws discussed below could discourage or make it more difficult to accomplish a proxy contest or other change in our management or the acquisition of control by a holder of a substantial amount of our voting stock. It is possible that these provisions could make it more difficult to accomplish, or could deter, transactions that stockholders may otherwise consider to be in their best interests or in our best interests. These provisions are intended to enhance the likelihood of continuity and stability in the composition of our board of directors and in the policies formulated by the

board of directors and to discourage certain types of transactions that may involve an actual or threatened change of control of us. These provisions are designed to reduce our vulnerability to an unsolicited acquisition proposal. The provisions also are intended to discourage certain tactics that may be used in proxy fights. Such provisions also may have the effect of preventing changes in our management.

Delaware Statutory Business Combinations Provision. We are subject to the anti-takeover provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is, or the transaction in which the person became an interested stockholder was, approved in a prescribed manner or another prescribed exception applies.

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For purposes of Section 203, a business combination is defined broadly to include a merger, asset sale or other transaction resulting in a financial benefit to the interested stockholder, and, subject to certain exceptions, an interested stockholder is a person who, together with his or her affiliates and associates, owns (or within three years prior, did own) 15% or more of the corporation s voting stock.

Classified Board of Directors; Removal of Directors for Cause. Our amended and restated certificate of incorporation and amended and restated bylaws provide that our board of directors is divided into three classes, each serving staggered three-year terms ending at the annual meeting of our stockholders. All directors elected to our classified board of directors will serve until the election and qualification of their respective successors or their earlier resignation or removal. The board of directors is authorized to create new directorships and to fill such positions so created and is permitted to specify the class to which any such new position is assigned. The person filling such position would serve for the term applicable to that class. The board of directors (or its remaining members, even if less than a quorum) is also empowered to fill vacancies on the board of directors occurring for any reason for the remainder of the term of the class of directors in which the vacancy occurred. Members of the board of directors may only be removed for cause and only by the affirmative vote of 80% of our outstanding voting stock. These provisions are likely to increase the time required for stockholders to change the composition of the board of directors. For example, in general, at least two annual meetings will be necessary for stockholders to effect a change in a majority of the members of the board of directors.

Advance Notice Provisions for Stockholder Proposals and Stockholder Nominations of Directors. Our amended and restated bylaws provide that, for nominations to the board of directors or for other business to be properly brought by a stockholder before a meeting of stockholders, the stockholder must first have given timely notice of the proposal in writing to our Secretary. For an annual meeting, a stockholder s notice generally must be delivered not less than 45 days nor more than 75 days prior to the anniversary of the mailing date of the proxy statement for the previous year s annual meeting. For a special meeting, the notice must generally be delivered by the later of 90 days prior to the special meeting or ten days following the day on which public announcement of the meeting is first made. Detailed requirements as to the form of the notice and information required in the notice are specified in the amended and restated bylaws. If it is determined that business was not properly brought before a meeting in accordance with our bylaw provisions, such business will not be conducted at the meeting.

Special Meetings of Stockholders. Special meetings of the stockholders may be called only by our board of directors pursuant to a resolution adopted by a majority of the total number of directors.

No Stockholder Action by Written Consent. Our amended and restated certificate of incorporation and amended and restated bylaws do not permit our stockholders to act by written consent. As a result, any action to be effected by our stockholders must be effected at a duly called annual or special meeting of the stockholders.

Super-Majority Stockholder Vote Required for Certain Actions. The Delaware General Corporation Law provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation s certificate of incorporation or bylaws, unless the corporation s certificate of incorporation or bylaws, as the case may be, requires a greater percentage. Our amended and restated certificate of incorporation requires the affirmative vote of the holders of at least 80% of our outstanding voting stock to amend or repeal any of the provisions discussed in this section of this prospectus entitled Anti-Takeover Provisions or to reduce the number of authorized shares of common stock or preferred stock. This 80% stockholder vote would be in addition to any separate class vote that might in the future be required pursuant to the terms of any preferred stock that might then be outstanding. In addition, an 80% vote is also required for any amendment to, or repeal of, our amended and restated bylaws by the stockholders. Our amended and restated bylaws may be amended or repealed by a simple majority vote of the board of directors.

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Outstanding Common Stock Purchase Agreement with Aspire Capital Fund

General

On December 14, 2012, we entered into a common stock purchase agreement (the **Purchase Agreement**) with Aspire Capital Fund, LLC (**Aspire Capital**). Upon execution of the Purchase Agreement, Aspire purchased 158,982 shares of common stock for an aggregate purchase price of $1.0 million based the closing price of our common stock December 13, 2012, the date upon which the business terms were agreed. Under the terms of the Purchase Agreement, Aspire has committed to purchase up to an additional 1,455,787 shares from time to time as directed by us over the next two years at prices derived from the market prices on or near the date of each sale. However, such commitment is limited to an additional $19.0 million of share purchases. In consideration for entering into the Purchase Agreement, concurrent with the execution of the Purchase Agreement, we issued to 74,548 shares of our common stock to Aspire in lieu of a commitment fee. Additionally, as of April 17, 2013, we issued approximately 650,000 shares of common stock, or an aggregate of $3.4 million to Aspire Capital under the Purchase Agreement.

Purchase of Shares under the Purchase Agreement

Under the Purchase Agreement, on any trading day selected by us on which the closing price of our common stock is not less than $1.00 per share, we may direct Aspire Capital to purchase up to 100,000 shares of our common stock per trading day so long as no sale pursuant to such Purchase Notice may exceed $500,000 per trading day. The Purchase Price of such shares is equal to the lesser of:

- the lowest sale price of our common stock on the purchase date; or

- the arithmetic average of the three lowest closing sale prices for our common stock during the twelve consecutive trading days ending on the trading day immediately preceding the purchase date.

In addition, on any date on which we submit a Purchase Notice to Aspire Capital in an amount equal to 100,000 shares we also have the right to direct Aspire Capital to purchase an amount of stock equal to up to 30% of the aggregate shares of the Company s common stock traded on The NASDAQ Capital Market on the next trading day, subject to the VWAP Purchase Share Volume Maximum and the VWAP Minimum Price Threshold, which is equal to the greater of (a) 90% of the closing price on the NASDAQ Global Market on the business day immediately preceding the VWAP Purchase Date or (b) such higher price as set forth by the Company in the VWAP Purchase Notice. The VWAP Purchase Price of such shares is the lower of:

(a) The closing sale price on the VWAP Purchase Date; or

(b) 96% of the volume-weighted average price for our common stock traded on the NASDAQ Global Market during normal trading hours:

- on the VWAP Purchase Date, if the aggregate shares traded on the NASDAQ Global Market have not exceeded the VWAP Purchase Share Volume Maximum; or

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- the portion of the VWAP Purchase Date until such time as the sooner to occur of (i) the time at which the aggregate shares traded on the NASDAQ Global Market has exceeded the VWAP Purchase Share Volume Maximum or (ii) the time at which the sale price of the common stock falls below the VWAP Minimum Price Threshold.

The Purchase Price will be adjusted for any reorganization, recapitalization, non-cash dividend, stock split, reverse stock split or other similar transaction occurring during the period(s) used to compute the Purchase Price. We may deliver multiple Purchase Notices and VWAP Purchase Notices to Aspire Capital from time to time during the term of the Purchase Agreement, so long as the most recent purchase has been completed.

Minimum Share Price

Under the Purchase Agreement, the Company and Aspire Capital may not effect any sales of shares of our common stock on any trading day that the closing sale price of our common stock is less than $1.00 per share.

Compliance with The NASDAQ Global Market Price

The Purchase Agreement provides that the number of shares that may be sold pursuant to the Purchase Agreement shall be limited to 1,689,317, or the Exchange Cap, which represents 19.99% of our outstanding shares as of December 14, 2012, unless shareholder approval or an exception pursuant to the rules of the NASDAQ Global Market is obtained to issue more than 19.99%, to be in compliance with the applicable listing maintenance rules of the NASDAQ Global Market. This limitation shall not apply if, at any time the Exchange Cap is reached and at all times thereafter, the average price paid for all shares issued and sold under the Purchase Agreement is equal to or greater than $6.29, the closing sale price of our common stock on December 14, 2012. We are not required or permitted to issue any shares of common stock under the Purchase Agreement if such issuance would breach our obligations under the rules or regulations of the NASDAQ Global Market. We currently do not intend to seek stockholder approval of the transactions contemplated by the Purchase Agreement.

Beneficial Ownership Limitation

Under the Purchase Agreement, the Company and Aspire Capital may not effect any sales of shares of our common stock if such shares proposed to be issued and sold, when aggregated with all other shares of our common stock beneficially owned by Aspire Capital and its affiliates, would result in the beneficial ownership by Aspire Capital and its affiliates of more than 19.99% of our then issued and outstanding shares of common stock.

Events of Default

Generally, Aspire Capital may terminate the Purchase Agreement upon the occurrence of any of the following events of default:

- the effectiveness of any registration statement that is required to be maintained effective pursuant to the terms of the Registration Rights Agreement between us and Aspire Capital lapses for any reason (including, without limitation, the issuance of a stop order) or is unavailable to Aspire Capital for sale of our shares of common stock, and such lapse or unavailability continues for a period of ten consecutive business days or for more than an

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aggregate of thirty business days in any 365-day period, which is not in connection with a post-effective amendment to any such registration statement; provided, however, that in connection with any post-effective amendment to such registration statement that is required to be declared effective by the SEC, such lapse or unavailability may continue for a period of no more than twenty consecutive business days, which such period shall be extended for an additional twenty business days if we receive a comment letter from the SEC in connection therewith;

- the suspension from trading or failure of our common stock to be listed on a Principal Market (as defined in the Purchase Agreement) for a period of three (3) consecutive business days;

- the delisting of our common stock from the NASDAQ Capital Market, provided our common stock is not immediately thereafter trading on the New York Stock Exchange, the NASDAQ Global Select Market, the NASDAQ Global Market, the NYSE Amex Equities or the OTCOB or OTCOX market places of the OTC markets;

- our transfer agent s failure to issue to Aspire Capital shares of our common stock which Aspire Capital is entitled to receive under the Purchase Agreement within five business days after an applicable purchase date;

- any breach by us of the representations, warranties, covenants or other term or condition contained in the Purchase Agreement or any related agreements that would reasonably be expected to have a material adverse effect except, in the case of a breach of a covenant which is reasonably curable, only if such breach continues for a period of at least five business days;

- if at any time the issuance of shares of common stock upon the submission of a Purchase Notice or VWAP Purchase Notice under this Agreement would result in the issuance of an aggregate of number of shares of common stock that would exceed the number of shares of common stock that we may issue under this agreement without breaching our obligations under the rules or regulations of the NASDAQ Global Market;

- if we become insolvent or are generally unable to pay our debts as they become due; or