Cyclacel Pharmaceuticals, Inc.
Form 424B3
April 27, 2012
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Registration No. 333-170 421

PROSPECTUS

Relating to the Resale of up to
4,371,121 Shares of Common Stock, $0.001 Par Value,
Comprised of:

(i) 209,526 Shares of Common Stock; and
(ii) up to 4,161,595 Shares of Common Stock
Issuable upon Exercise of Outstanding Warrants

CYCLACEL PHARMACEUTICALS, INC.

This prospectus relates to the resale or other disposition of 4,371,121 shares of common stock, par value $0.001 per share, by the selling stockholders identified herein, (i) 209,526 of which are issued and outstanding; and (ii) 4,161,595 of which are issuable upon exercise of five-year warrants to purchase common stock at an exercise price of $1.92 per share (the Warrants) that we issued as part of a private placement of our securities on October 7, 2010 (the Private Placement).

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

Our common stock is listed on the NASDAQ Global Market under the symbol CYCC. On April 26, 2012, the last reported sale price for our common stock was $0.59 per share.

Investing in our securities involves significant risks. We strongly recommend that you read carefully the risks we describe in this prospectus and the risk factors that are incorporated by reference in this prospectus from our filings made with the Securities and

Exchange Commission. See Risk Factors beginning on page 19 before deciding whether to invest in our securities.

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

The date of this prospectus is April 26, 2012.

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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 55. You should rely only on the information provided in this prospectus or documents incorporated by reference in this prospectus. We have not authorized anyone to provide you with different information. The information contained in this prospectus is accurate only as of the date of this prospectus and any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus or of any sale of our common stock. Our business, financial condition, results of operations and prospects may have changed since that date.

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

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PROSPECTUS SUMMARY

Because this is only a summary, it does not contain all of the information that may be important to you. You should carefully read the more detailed information contained in this prospectus and the information incorporated by reference carefully before you invest. Our business involves significant risks. You should carefully consider the information under the heading Risk Factors beginning on page 19.

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

Our Company

General

Cyclacel are cell cycle pioneers with a vision to improve patients healthcare with orally available innovative medicines. Our goal is to develop and commercialize small-molecule drugs that target the various phases of cell cycle control for the treatment of cancer and other serious diseases, particularly those of high unmet medical need.

Our strategy is to build a diversified biopharmaceutical business focused in hematology and oncology based on a portfolio of commercial products and a development pipeline of novel drug candidates. As a development stage enterprise, substantially all efforts of the Company to date have been devoted to performing research and development, conducting clinical trials, developing and acquiring intellectual property, raising capital and recruiting and training personnel.

Recent Developments

Purchase Agreement

On March 22, 2012, we entered into a purchase agreement with certain existing institutional stockholders and raised gross proceeds of $3,036,000 to fund certain litigation-related expenses on certain intellectual property and otherwise for general corporate purposes. Under the terms of the purchase agreement, the investors purchased 4,688,079 shares of the Company s common stock, par value $0.001 per share, or the Common Shares, at a per share purchase price of $0.6476, which is equal to the 10-day average closing price of the Company s common stock for the period ending on March 21, 2012, and obtained certain contractual economic rights, or the Economic Rights, generally related to the litigation, including rights to receive additional shares, or the Additional Shares, or warrants to purchase shares of common stock in certain circumstances. The Common Shares are subject to a lock-up for a period of one year from the date of issuance. The Economic Rights are transferable at any time to an affiliate of each respective investor, and are subject to a right of first refusal in favor of the Company with respect

to each proposed sale, transfer or other disposition.

The purchase agreement also provides for certain registration rights with respect to the Common Shares, and if issued, the Additional Shares. We are required, upon demand of a majority-in-interest of the investors, to use our commercially reasonable efforts to file a registration statement for the resale of such securities, and to cause such registration statement to be declared effective no later than 90 days following the date of such investors demand (or 180 days following such date, if the Securities and Exchange Commission determines to review the registration statement at issue). The investors are also entitled to piggyback registration rights, subject to cut-backs, as more fully set forth in the purchase agreement. We also agreed to other customary obligations regarding registration, including indemnification and maintenance of the effectiveness of the registration statements.

NASDAQ Appeal

As previously reported, on September 16, 2011, we received a letter from the NASDAQ stating that for 30 consecutive business days the bid price of our common stock had closed below $1.00 per share, the minimum closing bid price required by the continued listing requirements set forth in Listing Rule 5450(a)(1), or the Rule, and that, pursuant to Listing Rule 5810(c)(3)(A), we have 180 calendar days, or until March 14, 2012, to regain compliance with the minimum bid price requirement.

On March 15, 2012, we received a determination letter from NASDAQ notifying us that we had not regained compliance with the minimum closing bid price required by the continued listing requirements set forth in Listing Rule 5450(a)(1), or the Rule, during the 180 calendar days allowed to regain compliance pursuant to Listing Rule 5810(c)(3)(A), and that our security is subject to delisting from the NASDAQ Global Market, unless we timely request a hearing before a NASDAQ Listing Qualifications Panel, or the Panel. We have requested a hearing before the Panel to present our plan to regain compliance with the Rule, which request automatically stays the delisting of our securities pending the issuance of the Panel s decision. The hearing is scheduled for April 26, 2012.

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Under NASDAQ s Listing Rules, the Panel may, at its discretion, determine to continue our listing pursuant to an exception to the Rule for a maximum of 180 calendar days from the date of the NASDAQ Staff s notification, or through September 10, 2012. However, there can be no assurances that the Panel will do so.

Notwithstanding our request for a hearing before the Panel, if such appeal is unsuccessful, we may still transfer our listing to The NASDAQ Capital Market if it meets the initial listing criteria set forth in NASDAQ Marketplace Rule 5505, except for the bid price requirement. In that case, we may have an additional period of 180 calendar days in which to comply with the minimum bid price requirement. We currently meet these initial listing criteria, except for the bid price requirement.

Drug Candidates

The cell cycle, the process by which cells progress and divide, lies at the heart of cancer. In normal cells, the cell cycle is controlled by a complex series of signaling pathways by which a cell grows, replicated its DNA and divides. This process also includes mechanisms to ensure errors are corrected, and if not, the cells commit suicide (apoptosis). In cancer, as a result of genetic mutations, this regulatory process malfunctions, resulting in uncontrolled cell proliferation.

We have generated several families of anticancer drugs that act on the cell cycle including sapacitabine and seliciclib. We believe that these drug candidates are differentiated in that they are orally-available and interact with unique target profiles and mechanisms and have the potential to treat multiple cancer indications. CNDAC is incorporated into DNA during replication or repair, triggering a b-elimination reaction & leading to the formation of single-strand breaks (SSBs), which can activate the G2 checkpoint and/or be repaired by 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.

Our lead candidate, sapacitabine, is an orally-available prodrug of CNDAC, which is a novel nucleoside analog, or a compound with a structure similar to a nucleoside. A prodrug is a compound that has a therapeutic effect after it is metabolized within the body. CNDAC has a significantly longer residence time in the blood when it is produced in the body through metabolism of sapacitabine than when it is given directly. Sapacitabine acts through a novel dual mechanism whereby it interferes with DNA synthesis and repair by causing single-strand DNA breaks (SSBs) which can induce arrest of the cell division cycle at the G2/M checkpoint. During subsequent rounds of replication SSBs are converted to double-strand DNA breaks which may be repaired by the homologous recombination (HRR) pathway, or, if unrepaired, result in cell death. A number of nucleoside drugs, such as gemcitabine, or Gemzar®, from Eli Lilly, and cytarabine, also known as Ara-C, a generic drug, are in wide use as conventional chemotherapies. Both sapacitabine and its major metabolite, CNDAC, have demonstrated potent anti-tumor activity in both blood and solid tumors in preclinical studies. In a liver metastatic mouse model, sapacitabine was shown to be superior to gemcitabine and 5-FU, two widely used nucleoside analogs, in delaying the onset and growth of liver metastasis. We have retained worldwide rights to commercialize sapacitabine, except for Japan, for which Daiichi Sankyo Co., Ltd., or Daiichi Sankyo, has a right of first negotiation. 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 Acute Myeloid Leukemia, or AML, and Myelodysplastic Syndromes, or MDS. Sapacitabine is part of Cyclacel s pipeline of small molecule drugs designed to target and stop uncontrolled cell division.

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, non-small cell lung cancer, or NSCLC, and chronic lymphocytic leukemia, or CLL and in a Phase 1 study in solid tumors in combination with our own drug candidate, seliciclib.

Our second drug candidate, seliciclib, is a novel, first-in-class, orally-available, cyclin dependent kinase, or CDK, inhibitor. The compound selectively inhibits a spectrum of enzyme targets -CDK2, CDK7 and CDK9- that are central to the process of cell division and cell cycle control. The target profile of seliciclib is differentiated from the published target profile of other CDK inhibitors. Its selectivity is differentiated by publications by independent investigators which show 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. 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.

In addition to our lead development programs we have allocated limited resources to other programs allowing us to maintain and build on our core competency in cell cycle biology and related drug discovery. 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. In our second generation CDK inhibitor program, we have discovered several series of CDK inhibitors that we believe may prove to be more potent anticancer agents than seliciclib based on preclinical observations with our most advanced drug candidate being CYC065. In our polo-like kinase or Plk inhibitor program, CYC800, 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.

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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.

Lead Development Programs

Our pipeline and expertise in cell cycle biology

Our core area of expertise is in cell cycle biology and we focus primarily on the development of orally-available anticancer agents that target the cell cycle with the aim of slowing the progression or shrinking the size of tumors, and enhancing the quality of life and improving survival rates of cancer patients.

We have retained rights to commercialize our clinical development candidates and our business strategy is to enter into selective partnership arrangements with these programs.

Oncology Development Programs

We have generated several families of anticancer drugs that act on the cell cycle, including nucleoside analogues, CDK inhibitors, AK/VEGFR2 inhibitors and Plk inhibitors. Although a number of pharmaceutical and biotechnology companies are currently attempting to develop nucleoside analogues, CDK inhibitors, AK and/or VEGFR inhibitor drugs and Plk inhibitors, we believe that our drug candidates, are differentiated in that they are orally-available and demonstrate unique target profiles and mechanisms. For example, we believe that our sapacitabine is the only orally-available nucleoside analogue presently being tested in Phase 3 trials in AML and in Phase 2 for MDS.

In our development programs, we have been an early adopter of biomarker analysis to help evaluate whether our drug candidates are having their intended effect through their assumed mechanisms at different doses and schedules. Biomarkers are proteins or other substances whose presence in the blood can serve as an indicator or marker of diseases. Biomarker data from early clinical trials may also enable us to design subsequent trials more efficiently and to monitor patient compliance with trial protocols. We believe that in the longer term biomarkers may allow the selection of patients more likely to respond to its drugs for clinical trial and marketing purposes and increase the benefit to patients.

Research and Development Pipeline

The following table summarizes our currently active clinical and preclinical programs.

Program	Indication	Development Status	Target	Cell Cycle Mechanism
Oncology				
Sapacitabine, CYC682	Elderly AML	Phase 3 registration study on-going	DNA polymerase	G2 and S phase
Sapacitabine, CYC682	MDS	Phase 2 randomized trial on-going	DNA polymerase	G2 and S phase
Sapacitabine, CYC682	NSCLC	Phase 2 trial on-going	DNA polymerase	G2 and S phase
Sapacitabine, CYC682	CLL	Phase 2 randomized trial. Investigator-initiated study	DNA polymerase	G2 and S phase
Sapacitabine + Seliciclib	Cancer	Phase 1 trial on-going		

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Program	Indication	Development Status	Target	Cell Cycle Mechanism
Seliciclib, CYC202	NSCLC	Phase 2b randomized trial closed to accrual	CDK2, 7, 9	G1/S checkpoint and others
Seliciclib, CYC202	NPC	Phase 2 randomized trial. Lead-in phase only on-going	CDK2, 7, 9	G1/S checkpoint and others
Seliciclib, CYC065	Cancer	Preclinical	CDK2, 5, 9	G1/S checkpoint and others
Plk1 Inhibitors	Cancer	Preclinical	Plk	G2/M checkpoint
Other therapeutic areas				
Cell Cycle Inhibitors	Autoimmune & Inflammatory Diseases	Phase 1 trial completed On hold. Not a company priority	CDK	G1/S checkpoint and others

Market opportunity in oncology

Cancer remains a major life-threatening disease in the United States with approximately 3.2 million people afflicted by cancer and approximately 1.4 million new cases of cancer diagnosed every year.

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

The American Cancer Society estimates that approximately 16,000 to 20,000 new cases of myelodysplastic syndromes are diagnosed annually in the United Sates. Patients currently receive hypomethylating agents as first-line treatment. There is no approved therapy for second-line treatment.

Five common solid cancer types: non-small cell lung, breast, ovarian, prostate and colorectal cancers, represent over 50% of all new cases of cancer in the United States each year and account for more than 50% of all cancer deaths in the United States.

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 dual mechanism whereby the compound interferes with DNA synthesis through the incorporation of CNDAC into DNA and repair by causing DNA single-strand breaks. This leads to the production of DNA double strand breaks (DSBs) and/or checkpoint activation at G2/M checkpoint. Unrepaired DSBs cause cell death. Repair of sapacitabine-induced DSBs is dependent on the Homologous Recombinant Repair pathway.

We are currently exploring sapacitabine in both hematological cancers and solid tumors. To date, sapacitabine has been evaluated in approximately 400 patients in several Phase 1 and 2 studies and has shown signs of anti-cancer activity. The SEAMLESS pivotal Phase 3 trial is on-going, which evaluates sapacitabine oral capsules as a front-line treatment in elderly patients aged 70 years or older with newly-diagnosed AML who are not candidates for intensive induction chemotherapy. The study will be conducted under an SPA. An SPA provides trial sponsors with an FDA agreement that the design and analysis of the trial adequately address objectives in support of a submission for a marketing application if the trial is performed according to the SPA. The SPA may only be changed through a written agreement between the sponsor and the FDA or if the FDA becomes aware of a substantial scientific issue essential to product efficacy or safety. However, an SPA does not provide any assurance that a marketing application would be approved by the FDA.

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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

SEAMLESS is our pivotal Phase 3 trial for sapacitabine oral capsules as a front-line treatment of elderly patients aged 70 years or older with newly diagnosed AML who are not candidates for intensive induction chemotherapy. The study is being conducted under an SPA agreement that Cyclacel reached with the FDA. SEAMLESS builds on promising 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. SEAMLESS will be monitored by a Data Safety Monitoring Board, or DSMB. A prespecified interim analysis for futility will be performed and reviewed by the DSMB. In October 2011, the DSMB reviewed the lead-in arm of the study, which followed the same treatment regimen as Arm A, and recommended that the study should enter the randomized stage as planned and following this recommendation we have implemented an improvement in the SEAMLESS trial design converting it into the two-arm design described above from the original three-arm design. We received written confirmation from the FDA that, following the modification in the trial design, the previously agreed SPA agreement remains valid.

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 2011 American Society of Hematology, or ASH, Annual Meeting in San Diego, California. The study enrolled 25 patients aged 70 years or older, 76% of which were aged 75 years or older. Thirty-day mortality from all causes was 4% and 60-day mortality from all causes 12%. The overall response rate was 40%. We reported median overall survival at 231 days with 44% of patients still alive. No dose-limiting toxicities were observed in 25 patients. The median age in the group is 76 years (range 72-90). Nineteen patients were 75 years or older (76%). Common adverse events regardless of cause included anemia, asthenia, decreased appetite, diarrhea, constipation, dyspnea, limb edema, hypocalcemia, nausea, febrile neutropenia, neutropenia, lung infection, and thrombocytopenia, which were mostly moderate in intensity.

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

In December 2007, we initiated an open-label, multicenter, randomized Phase 2 clinical trial of oral sapacitabine in 60 elderly patients with AML aged 70 or older who are previously untreated or in first relapse. The Phase 2 study, led by Dr. Kantarjian, has a primary endpoint of 1-year survival rate of three dosing schedules of sapacitabine in elderly patients with previously untreated or first relapsed AML. Secondary objectives are to assess complete remission, or CR, partial remission, or PR, duration of CR or CRp, or major hematological improvement and their corresponding durations, transfusion requirements, number of hospitalized days and safety. The study uses a selection design with the objective of identifying a dosing schedule among three different arms, A. 200 mg twice daily for seven days every 3-4 weeks, B. 300 mg twice daily for seven days every 3-4 weeks, and C. 400 mg twice daily for three days per week for two weeks every 3-4 weeks, which produces a better one year survival rate in the event that all three dosing schedules are active. Each arm enrolled and treated 20 patients. Approximately 55% of patients had AML de novo and the rest had AML preceded by antecedent hematological disorder, or AHD, such as MDS, or myeloproliferative disease. Eighty percent of the patients were untreated and 20% in first relapse. We completed enrollment of 60 AML patients

in this study in October 2008. In December 2009, at the 51st ASH Annual Meeting we reported one year survival data.

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

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

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

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

Sapacitabine is in Phase 2 development as a second-line treatment in patients aged 60 or older with MDS who are previously treated with hypomethylating agents. The MDS stratum of the study is designed as a protocol amendment expanding the ongoing Phase 2 trial of sapacitabine in AML described above, to include a cohort of patients with MDS. Patients with MDS often progress to AML. The primary objective of the MDS stratum is to evaluate the one year survival rate of three dosin