Cyclacel Pharmaceuticals, Inc.
Form 424B5
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Registration Statement No. 333-211046
PROSPECTUS SUPPLEMENT
(To Prospectus Dated June 8, 2016)

Cyclacel Pharmaceuticals, Inc.
Up to $4,000,000
COMMON STOCK

We have entered into an At Market Issuance Sales Agreement, which we refer to as the sales agreement, with FBR Capital Markets & Co., or FBR, dated June 23, 2016, relating to the sale of shares of our common stock offered by this prospectus supplement. In accordance with the terms of the sales agreement, under this prospectus we may offer and sell shares of our common stock, $0.001 par value per share, having an aggregate offering price of up to $4.0 million from time to time through FBR, acting as agent.

Our common stock is listed on The NASDAQ Capital Market under the symbol “CYCC.” On June 22, 2016, the last reported sale price of our common stock was $5.22 per share.

Sales of our common stock, if any, under this prospectus supplement will be made by any method permitted that is deemed an “at the market offering” as defined in Rule 415 under the Securities Act of 1933, as amended, or the Securities Act, including sales made directly on or through the NASDAQ Capital Market, the existing trading market for our common stock, sales made to or through a market maker other than on an exchange or otherwise, in negotiated transactions at market prices, and/or any other method permitted by law. FBR is not required to sell any specific amount, but will act as our sales agent using commercially reasonable efforts consistent with their normal trading and sales practices. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

FBR will be entitled to compensation at a commission rate equal to 3% of the gross sales price per share sold. In connection with the sale of the common stock on our behalf, FBR may be deemed to be an “underwriter” within the meaning of the Securities Act and the compensation of FBR may be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to FBR with respect to certain liabilities, including liabilities under the Securities Act.

On May 27, 2016, we implemented a one-for-twelve reverse stock split of our issued and outstanding shares of common stock, or the Reverse Stock Split. The Reverse Stock Split became effective at the opening of trading on The NASDAQ Capital Market on May 31, 2016. All references in this prospectus supplement to number of shares of common stock, price per share and weighted average shares of common stock have been adjusted to reflect the Reverse Stock Split on a retroactive basis for all periods presented, unless otherwise noted.

The aggregate market value of our outstanding shares of common stock held by non-affiliates was $16,076,501 based on 3,007,204 shares of common stock outstanding, as of the date of this prospectus, of which 2,500,234 shares were held by non-affiliates, and a per share price of $6.43 based on the closing sale price of our common stock on the NASDAQ Capital Market on June 6, 2016 (after giving effect to the Reverse Stock Split). Under the registration statement to which this prospectus supplement forms a part, we may not sell our securities in a primary offering with a value exceeding one-third of our public float in any 12-month period (unless our public float rises to $75.0 million or more). During the prior 12 month calendar period that ends on, and includes, this prospectus supplement, we have sold securities having an aggregate market value of approximately $1,101,984 pursuant to General Instruction I.B.6 of Form S-3. Accordingly, we may sell up to approximately $4,256,850 in shares of common stock hereunder.

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 S-13 of this prospectus supplement and page 14 of the accompanying prospectus and in the documents incorporated by reference into this prospectus supplement and the accompanying prospectus under the caption "Risk Factors."

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

The date of this prospectus supplement is June 23, 2016.

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Prospectus Supplement

Prospectus

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ABOUT THIS PROSPECTUS SUPPLEMENT

You should rely only on the information contained in or incorporated by reference in this prospectus supplement, the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering. We have not, and FBR has 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 are not, and FBR is not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted or in which the person making that offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make an offer or solicitation. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering, is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering, in their entirety before making an investment decision. You should also read and consider the information in the documents to which we have referred you in the sections of this prospectus supplement entitled “Where You Can Find More Information” and “Incorporation of Documents by Reference.”

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 in this prospectus supplement and the accompanying prospectus. The second part, the accompanying prospectus dated June 8, 2016, including the documents incorporated by reference therein, provides more general information, some of which may not apply to this offering. 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, 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. 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 the accompanying prospectus — 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.

In this prospectus supplement, “we,” “us,” “our,” “the company” and “Cyclacel” refer to Cyclacel Pharmaceuticals, Inc., unless the context otherwise requires.

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PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights information contained elsewhere or incorporated by reference in this prospectus supplement and the accompanying prospectus. This summary does not contain all of the information that you should consider before deciding to invest in our common stock. You should read this entire prospectus supplement and the accompanying prospectus carefully, including the "Risk Factors" section contained in this prospectus supplement, our consolidated financial statements and the related notes thereto and the other documents incorporated by reference in this prospectus supplement and the accompanying prospectus.

Overview

We are a biopharmaceutical company dedicated to the development and commercialization of novel, mechanism-targeted drugs to treat human cancers and other serious diseases. Our strategy is to build a diversified biopharmaceutical business in hematology and oncology based on a development pipeline of novel drug candidates.

Drug Candidates

The cell cycle, the biological process by which cells propagate 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, replicates its DNA and divides. This process also includes mechanisms to ensure errors are corrected, and if not, the cells commit suicide or apoptose. 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, seliciclib and CYC065. 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.

Our lead candidate, sapacitabine, is a novel, orally-available nucleoside analog. A number of nucleoside drugs, such as gemcitabine and cytarabine, also known as Ara-C, both generic drugs, 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 fluorouracil, or 5-FU, two widely used nucleoside analogs, in delaying the onset and growth of liver metastasis. We hold the 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.

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 a Phase 2 study for MDS and in a Phase 1/2 study in solid tumors in combination with seliciclib, another of our drug candidates. Sapacitabine has been evaluated in approximately 1,000 patients to date.

In Cyclacel's second development program the Company is evaluating CDK inhibitors. CDKs are involved in cancer cell growth, survival, metastatic spread and DNA damage repair. Seliciclib, Cyclacel's lead CDK inhibitor, is an oral, highly selective inhibitor of CDK enzymes that are central to the process of cell division and cell cycle control. Seliciclib is currently being evaluated in an oral regimen in combination with sapacitabine in a Phase 1/2 study of patients with Homologous Recombination (HR) repair-deficient breast, ovarian and pancreatic cancers, including BRCA positive tumors. An extension cohort of BRCA positive breast cancer patients is on-going. Seliciclib has been evaluated in over 450 patients with various cancers, including a Phase 2b randomized study in third-line non-small cell lung cancer , or NSCLC, and nasopharyngeal cancer, or NPC, and has shown signs of anticancer activity. Cyclacel has retained worldwide rights to commercialize seliciclib. Seliciclib is also being evaluated in Investigator Sponsored Trials, or ISTs, to treat Cushing's disease and rheumatoid arthritis, or RA and in a licensing and supply agreement to treat cystic fibrosis.

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Cyclacel's second generation CDK inhibitor, CYC065, is a highly selective inhibitor of CDKs targeting CDK2/9 enzymes with potential utility in both hematological malignancies and solid tumors. CYC065 has increased anti-proliferative potency and improved pharmaceutical properties compared to seliciclib. CYC065 is in an on-going first-in-human, Phase 1 trial to assess its safety, tolerability, pharmacokinetics and pharmacodynamics in advanced cancer patients. CYC065 was selected from the Company's drug discovery program in Dundee, Scotland.

In addition to these development programs, in our polo-like kinase, or PLK, inhibitor program, we have discovered CYC140 and other potent and selective small molecule inhibitors of PLK1, a kinase that is active during cell division and which targets the mitotic phase of the cell cycle. PLK was discovered by Professor David Glover, our Chief Scientist. We have received a grant award of approximately $3.5 million from the Biomedical Catalyst of the United Kingdom government to complete IND-directed preclinical development of CYC140.

We currently retain virtually all marketing rights worldwide to the compounds associated with our drug programs. To optimize our commercial return, we intend to enter into selected partnering arrangements.

Clinical 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.

Oncology Development Programs

We have generated several families of anticancer drugs that act on the cell cycle, including nucleoside analogs, CDK inhibitors, PLK inhibitors and Aurora Kinase/vascular endothelial growth factor receptor, or AK/VEGFR inhibitors. 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 biological substances or effects whose presence in patient samples can serve as an indicator or marker of diseases, or may highlight patients more likely to respond to a particular treatment. Biomarker data from early clinical trials may also enable us to design subsequent trials more efficiently and to monitor patient compliance with trial protocols. For example, we reported that sapacitabine efficacy is enhanced in tumor cells that are defective in homologous recombination DNA repair and that sapacitabine treatment increased a DNA damage marker in patient samples. We believe that in the longer term biomarkers may allow the selection of patients more likely to respond to our drugs in clinical trials and increase the benefit to patients.

Although a number of pharmaceutical and biotechnology companies are currently attempting to develop nucleoside analogs, CDK inhibitors 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 analog presently being tested in a Phase 3 trial in previously untreated AML and in Phase 2 for high risk MDS.

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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. Enrollment completed	DNA polymerase	G2 and S phase
Sapacitabine, CYC682	MDS	Phase 2 randomized trial Enrollment completed	DNA polymerase	G2 and S phase
Seliciclib + Sapacitabine	Cancer	Phase 1/2 trial on-going		
CYC065 CDK inhibitor	Cancer	Phase 1 first-in-human solid tumors and lymphoma; on-going	CDK2/9	G1/S checkpoint and others
CYC140 PLK inhibitor	Cancer	Preclinical	PLK1	G2/M checkpoint
Investigator Sponsored Trials				
Seliciclib, CYC202	Cushing's disease and rheumatoid arthritis	Phase 2 trial	CDK2/9	G1/S checkpoint and others
Licensing & Collaboration				
Seliciclib, CYC202	Cancer	Phase 2 trial		

Market opportunity in hematology

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.

AML is a cancer of the blood cells that progresses rapidly and if not treated, could be fatal within a few months. AML is generally a disease of older people and is uncommon before the age of 40. The average age of a patient with AML is about 67 years. According to The Surveillance, Epidemiology, and End Results, or SEER, program of the National Cancer Institute, or NCI, the incidence rate of AML is approximately 20,000 in the United States. It is estimated that European incidence is approximately 22,000. A review of The University of Texas MD Anderson Cancer Center's historical experience with front-line intensive induction chemotherapy for AML patients aged 70 years or older demonstrated that while 45% achieved a complete remission, median overall survival was only 4.6 months and was associated with a 4-week death rate of 26% and an 8-week death rate of 36%.

MDS is a family of clonal myeloid neoplasms, or malignancies of the blood, caused by the failure of blood cells in the bone marrow to develop into mature cells. Patients with MDS typically suffer from bone marrow failure and cytopenias, or reduced counts of platelets, red and white blood cells. The exact incidence and prevalence of MDS are unknown because it can go undiagnosed and a national survey canvassing both hospitals and office practitioners has not been completed. Some estimates place MDS incidence at 15,000 to 20,000 new cases each year in the United States alone with some authors estimating incidence as high as 46,000. Literature suggests that there is a rising incidence of MDS as the age of the population increases with the majority of patients aged above 60 years. Patients currently receive hypomethylating agents as first-line treatment. There is no approved therapy for second-line treatment.

Sapacitabine

Sapacitabine, previously known as CYC682, is an orally-available nucleoside analog. 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

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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 beta-elimination reaction and leading to the formation of single-strand DNA breaks, or SSBs. During subsequent rounds of replication, SSBs are converted to double-strand breaks, or DSBs; these can be repaired by the homologous recombination repair, or HRR, pathway, or, if unrepaired, result in cell death.

We are currently exploring sapacitabine in both hematological cancers and solid tumors. Approximately 1,000 patients have received sapacitabine in Phase 1, 2 and 3 studies.

Hematological Cancers

SEAMLESS, randomized Phase 3, pivotal trial of sapacitabine in elderly patients with AML

The SEAMLESS study is being conducted under an SPA agreement that Cyclacel reached with the FDA.

The study is chaired by Hagop M. Kantarjian, M.D., Chairman and Professor, Department of Leukemia, The University of Texas MD Anderson Cancer Center. SEAMLESS is a multicenter, randomized, Phase 3 study of sapacitabine as a front-line treatment in approximately 485 elderly patients aged 70 years or older with newly diagnosed AML who are not candidates for or have refused intensive induction chemotherapy. In SEAMLESS an investigational arm of oral sapacitabine administered in alternating cycles with intravenous decitabine is compared with a control arm of intravenous decitabine administered alone. The primary efficacy endpoint is overall survival.

SEAMLESS completed enrollment in December 2014 with approximately 110 centers participating from the United States and Europe. Also in December 2014, the Data Safety Monitoring Board, or DSMB, conducted a planned interim analysis for futility after 247 events, or patient deaths, and the final safety review of 470 randomized patients. The DSMB found no safety concerns. However, the planned futility boundary has been crossed and the DSMB determined that, based on available interim data, it would be unlikely for the study to reach statistically significant improvement in survival. The DSMB saw no reasons why patients should discontinue treatment on their assigned arm and recommended that recruited patients stay on treatment.

The interim analysis for futility performed in December 2014 was primarily driven by the events within the first 6 months of patients entering into the trial. Of 247 events in SEAMLESS, 173 (70%) have occurred in the first 6 months. This means that the survival curves beyond 6 months are poorly estimated at the time of the analysis. Furthermore, follow up of European patients at December 2014 is significantly shorter than that of U.S. patients as the study opened for European accrual in April 2014. It is important to have complete follow up of all patients to ensure that a potential treatment effect beyond 6 months is not missed.

In accordance with the DSMB’s recommendations, we continue to follow-up patients as per the study protocol until the prespecified 424 events have been observed. This is estimated to occur around the end of the first half of 2016. Approximately 2.6% of the prespecified events remain to be observed as of May 11, 2016.

In parallel to the follow-up of enrolled patients we have submitted, and have received validation of, a Pediatric Investigation Plan, or PIP, to the EMA. The EMA requires sponsors to agree to a PIP before a marketing authorization application, or MAA, can be accepted, and because the lead times can be long, we submitted the PIP ahead of any MAA submission. Depending on the final data, we may meet with regulatory authorities in Europe and the United States to discuss registration submissions for sapacitabine for the AML indication.

Pilot/Lead-in study of sapacitabine in elderly patients with AML

Results from a single-arm, multicenter, Phase 1/2 clinical trial examining the safety and efficacy of oral sapacitabine administered sequentially with intravenous decitabine, the same regimen as in the investigational arm of SEAMLESS, were reported during a poster session at the 2012 American Society of Hematology, or ASH, Annual Meeting. 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

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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 one-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 study of sapacitabine in patients with previously untreated or first relapse AML

SEAMLESS builds on promising one year survival observed in elderly patients with AML enrolled in a Phase 2 study of single agent sapacitabine. In December 2007, we initiated a multicenter, randomized Phase 2 clinical trial of oral sapacitabine in 60 elderly patients with AML aged 70 years or older who were previously untreated or in first relapse. The Phase 2 study, led by Dr. Kantarjian, had a primary endpoint of one year survival and randomized patients to one of three dosing schedules of sapacitabine. Secondary objectives were to assess complete remission, or CR, partial remission, or PR, duration of CR or CRp, or major hematological improvement and their corresponding durations, transfusion requirements, number of hospitalized days and safety. The study used 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 would produce a better one year survival rate in the event that all three dosing schedules were 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. Between December 27, 2007 and April 21, 2009, a total of 105 patients were enrolled and treated in the Phase 2 study. Their median age was 77 years with a range of 70-91 years. 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 was assigned to one of three dosing schedules: 200 mg twice a day for 7 days (Arm A); 300 mg twice a day for 7 days (Arm B); and 400 mg twice a day for 3 days each week for 2 weeks (Arm C). All schedules were given in 28 day cycles. The 3-day dosing schedule in Arm 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 one-year survival rate of 30%, median overall survival of 213 days and durable complete remissions, or CRs, in 25% of patients. The median overall survival of patients from all arms 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.

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, or 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 one-year survival with the objective of identifying a dosing schedule that produces a better one-year survival rate in the event that all three dosing schedules are active. All patients in

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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 December 2013 at the 2013 ASH Meeting and Exposition, we announced primary endpoint data from the ongoing, open-label, multicenter, randomized Phase 2 trial of oral sapacitabine capsules in older patients with myelodysplastic syndromes after treatment failure of front-line hypomethylating agents, such as azacitidine and/or decitabine. The median overall survival for each arm was approximately 9.7 months for Arm G, 9.7 months for Arm H, and 7.6 months for Arm I. The median overall survival for all three arms was approximately 8.6 months. One-year survival was 38% for Arm G, 24% for Arm H, and 33% for Arm I. Nine patients had responded (2 CRs, 2 CRp, and 5 major HIs): 19% for Arm G, 10% for Arm H and 14% for Arm I and the time to response was one to four cycles. Median number of cycles was three with a range of one to over 23 and 30 patients received four or more cycles. Additionally, 23 patients achieved stable disease lasting longer than 16 weeks. The 30 day mortality from all causes was 5% in each of the three arms and ten patients, or approximately 16%, were still alive.

We have recently completed enrollment of a patient cohort in an additional part of the MDS Phase 2 study in order to evaluate better dosing regimens. We will follow-up these additional Phase 2 patients until mature survival data become available. In parallel, we anticipate initiating a Phase 1/2 trial of sapacitabine in combination with other agents to determine safety and tolerability. We would expect to plan a Phase 2 randomized controlled trial, or RCT, of sapacitabine in combination with other agents following a review of all relevant clinical data with mature follow-up. Median overall survival after treatment failure of front-line hypomethylating agents, such as azacitidine and/or decitabine, for patients with intermediate-2 or high- risk disease per IPSS, is reported in the literature to range between 5.9 and 4.3 months. Patients with high-risk 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.

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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Cyclin Dependent Kinase Inhibitor program

Cyclin Dependent Kinase Inhibitors, or CDKs, are enzymes that are central to the process of cell division and cell cycle control and play pivotal roles in cancer cell growth, survival and DNA damage repair. Inhibition of CDKs 2 and 9 may also overcome aberrant cell cycle control in certain non-malignant diseases of proliferation.

Seliciclib

Seliciclib, is a novel, orally-available, CDK2/9 inhibitor which has a target profile 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 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 over 450 patients in several Phase 1 and 2 studies, including studies in NSCLC and NPC, and has shown signs of anti-cancer activity. We have retained worldwide rights to commercialize seliciclib.

DNA damage response program: Phase 1/2 clinical trial of seliciclib and sapacitabine in patients with advanced cancers

An ongoing Phase 1, dose escalation study conducted in patients with advanced and incurable solid tumors. The orally-administered regimen consists of sapacitabine administered twice daily for 7 days sequentially followed by seliciclib twice daily for 3 days over a 21 day cycle (Part 1, n=38); and sapacitabine dosed each morning followed by seliciclib each evening, each once daily for 5 days per week for 2 weeks of a 28 day cycle (Part 2, n=29). The primary objective of the trial is to determine the maximum tolerated dose with a secondary objective of antitumor activity of the combination. Sixty-seven patients have been treated in Parts 1 and 2 of the study, of which 44 were found to carry BRCA mutations and one a sporadic BRCA mutation.The study is being conducted at Dana Farber Cancer Institute in Boston and the principal investigator is Geoffrey I. Shapiro, MD with participation from other Harvard Medical School hospitals.

At the 2016 American Society of Clinical Oncology Annual Meeting, or ASCO, Sara M. Tolaney, M.D., M.P.H., Associate Director, Clinical Research, Breast Oncology, Dana-Farber Cancer Institute, Boston reported in an oral presentation that one complete response and five partial responses were observed in BRCA mutation carriers with breast, ovarian and pancreatic cancers. Treatment durations for the three breast/ovarian cancer responders in Part 1 are 54, 93, over 240 weeks and the one breast cancer responder in Part 2 over 76 weeks respectively. Treatment durations for the two pancreatic cancer responders, one each in Parts 1 and 2, are 21 and 16 weeks respectively. Responders included patients who underwent prior treatment with PARP inhibitors and PARP naïve patients. Stable disease was observed in nine BRCA mutation carriers and one sporadic BRCA positive patient with treatment durations ranging from 16 to 88 weeks.

Overall in BRCA positive patients (Parts 1 and 2, n=45), disease control rate is 35.6% and overall response rate, or ORR, is 11% (Part 1 ORR 25% and Part 2 7%). The difference in Part 1 and Part 2 ORRs may suggest that the seliciclib dose in the Part 2 schedule may be too low for enhancing the activity of sapacitabine.

Pharmacodynamic effects of the seliciclib and sapacitabine combination were observed in skin biopsies. Part 1 biopsies following 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.

In Part 1 recommended Phase 2 doses, or RP2D, are: sapacitabine 50 mg b.i.d./seliciclib 800 mg b.i.d. Most frequent grade 3/4 adverse events were neutropenia (16%) and elevation in AST (16%). In Part 2 RP2D are: sapacitabine 250 mg q.d./seliciclib 200 mg q.d. Most frequent grade 3/4 adverse events were neutropenia (28%) and elevation in AST (10%). Dose limiting toxicities were reversible elevations in transaminase and bilirubin, neutropenia or febrile neutropenia and pneumonia.

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Based on encouraging results from the initial patients and investigator interest the study has been expanded to evaluate an additional 20 breast cancer patients all of whom are required to test positive for BRCA in baseline biopsies. Patients will also undergo whole exome sequencing with the objective of further characterizing the genetic profiles of their tumors.

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.

CYC065

CYC065 is a highly-selective, second generation inhibitor of CDK2 and CDK9 that causes apoptotic death of cancer cells at sub-micromolar concentrations and is bioavailable via oral and intravenous routes. Antitumor efficacy has been achieved in vivo with once a day oral dosing at well tolerated doses. Evidence from published preclinical studies show that CYC065 may benefit patients with adult and pediatric hematological malignancies, including certain AML, Acute Lymphocytic Leukemias, or ALL, Chronic Lymphocytic Leukemias, or CLL, Diffuse Large B-cell Lymphoma, or DLBCL, Multiple Myelomas or MM, and certain solid tumors, including breast and uterine cancers.

CYC065 is in an on-going, first-in-human, Phase 1 trial to assess its safety, tolerability, pharmacokinetics and pharmacodynamics in solid tumor and lymphoma patients. The trial is being conducted at the Dana Farber Cancer Institute in Boston and the principal investigator Dr Geoffrey I. Shapiro, M.D. CYC065 was selected from the Company's drug discovery program in Dundee, Scotland and its development was supported in part by a grant award of approximately $1.9 million from the Biomedical Catalyst of the United Kingdom government.

CYC065 is mechanistically similar but has much higher dose potency, in vitro and in vivo, improved metabolic stability and longer patent protection than seliciclib, Cyclacel's first generation CDK2/9 inhibitor. Translational biology data support development of CYC065 as a stratified medicine for solid and liquid tumors. CYC065 has been shown to reverse drug resistance associated with the addiction of cancer cells to cyclin E, a partner protein of CDK2, and inhibit CDK9-dependent oncogenic and leukemogenic pathways, including MYC and multilineage leukemia rearrangements, or MLL-r. Like seliciclib, CYC065 also represses the MCL-1-mediated survival pathway in cancer cells, leading to rapid induction of apoptosis in MCL-1 dependent cancer cells.

In 2011, independent investigators published preclinical evidence that CYC065 as a single-agent can induce tumor growth delay in HER2-positive breast cancer cells addicted to cyclin E and resistant to trastuzumab, or Herceptin®, while administration of CYC065 in combination with trastuzumab resulted in regression or sustained tumor growth inhibition.

Data presented at the American Association for Cancer Research, or AACR, 2016 Annual Meeting demonstrated the therapeutic potential of CYC065 as a targeted anti-cancer agent. The preclinical data shows that CYC065 can induce cell death, and that it combined beneficially with anti-cancer drugs from the Bcl-2 and BET inhibitor classes, in in vitro models of B-cell lymphoma, including double-hit lymphomas. The preclinical study evaluated both single-agent activity of CYC065 and combinations of CYC065 with the Bcl-2 inhibitor, venetoclax (ABT-199, Venclexta®), and BET (Bromodomain and Extra-Terminal) inhibitors in B-cell lymphoma cell lines. Short exposure to CYC065 was sufficient to downregulate MYC, an oncogene aberrantly expressed in many cancers, and Mcl-1, an anti-apoptotic member of the Bcl-2 family, and to induce cell death. CYC065 treatment had no impact on Bcl-2 levels. Combinations of CYC065 with venetoclax or BET inhibitors were both synergistic. CYC065 targets key oncogenic and survival pathways in double-hit B-cell lymphomas suggesting a therapeutic rationale for this indication. Additionally, data presented at the 2015 Annual Meeting of the American Association of Cancer Research, or AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics demonstrated the mechanistic rationale for clinical development of CYC065 in oncology. Data

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showed that MLL gene status and levels of Bcl-2 family proteins correlated with sensitivity of AML cell lines to CYC065. Combination studies revealed the potential to combine CYC065 with available and experimental leukemia therapies, including cytarabine and Bcl-2 inhibitors. Potent anticancer activity of CYC065 was demonstrated in vivo in AML xenograft models resulting in over 90% inhibition of tumor growth. The potent in vitro and in vivo anti-cancer activity, opportunity for patient stratification and the ability to combine with anti-leukemic agents suggest that CYC065 may have therapeutic potential in AML.

Data presented at the 2015 San Antonio Breast Cancer Symposium demonstrated in particular the mechanistic rationale for clinical development of CYC065 in basal-like triple negative breast cancer, or TNBC, a cancer with poor prognosis frequently associated with BRCA mutations. Molecular characteristics of TNBC include amplification or overexpression of Cyclin E, the partner protein of CDK2, and MYC. CYC065 directs a pro-apoptotic mechanism in breast cancer cell lines, which includes transcriptional down regulation of key pro-survival and oncogenic regulators, including MCL-1 and MYC.

CYC065 was shown to rapidly induce cell death in breast cancer cell lines, while transiently inducing G1 cell cycle arrest in non-malignant breast lines. CYC065's potent anticancer activity has been confirmed in breast cancer xenograft animal models. Like seliciclib, CYC065 effectively combined with sapacitabine in breast cancer cell lines.

In 2015, independent investigators presented data demonstrating that CYC065 prolongs survival in MYCN-addicted neuroblastoma models. The study evaluated the ability of CYC065 to inhibit cell proliferation and induce apoptosis of neuroblastoma cells in vitro and in vivo. In vivo efficacy was evaluated in subcutaneous xenograft models of both MYCN-amplified and non-amplified neuroblastoma cells and the Th-MYCN genetically-engineered mouse model of neuroblastoma. The study showed that neuroblastoma cell lines with MYCN amplification and high MYCN expression levels were sensitive to the CYC065 inhibitor. CYC065 also depleted MYCN protein in a time- and dose-dependent manner, blocked neuroblastoma cell proliferation and induced apoptosis which resulted in significantly reduced tumor burdens and prolonged survival in MYCN-addicted neuroblastoma models in vivo.

Similar to palbociclib, a drug which targets CDK4/6 and the first CDK inhibitor to be recently approved by the FDA, we anticipate that CYC065 will likely be best used in combination with available anti-cancer agents. Depending on the data from the ongoing Phase 1 study, we are also interested in evaluating CYC065 in patients with hematological malignancies in light of profound signals of activity observed in preclinical studies.

PLK inhibitors

In our PLK inhibitor program we have discovered potent and selective small molecule inhibitors of PLK1, a kinase active during cell division, which target the mitotic phase of the cell cycle. At the 2012 Annual Meeting of the AACR, we reported that one of these compounds, CYC140, was selected for further preclinical development and showed potent activity and selectivity against a panel of esophageal cancer cell lines. 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. PLK was discovered by Professor David Glover, our Chief Scientist. We have received a grant award of approximately $3.5 million from the Biomedical Catalyst of the United Kingdom government to complete IND-directed preclinical development of CYC140.

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. Vascular endothelial growth factor receptor 2, or VEGFR2 is a receptor protein that plays a key regulatory role in the angiogenesis pathway, or blood vessel formation. VEGFR is targeted by approved drugs such as bevacizumab and sorafenib indicated for the treatment of several solid cancers, such as breast, colorectal, kidney, liver and lung.

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At the Annual Meeting of the AACR 2012 we reported that collaborators tested the activity of CYC3, our novel Aurora Kinase A specific inhibitor, in pancreatic cancer cell lines and found that CYC3 acted 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. The collaborators reported that the combination merits further investigation and has the potential for improved therapeutic index in vivo. We have 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, but have no current plans to progress the program. We have retained worldwide rights to commercialize CYC116 and our other Aurora kinase inhibitors.

Investigator-Sponsored Trials

Preclinical results from several independent investigators suggest that cell cycle inhibitors, such as seliciclib and related 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 glomerulonephritis, graft-versus-host disease, idiopathic pulmonary fibrosis, lupus nephritis, polycystic kidney disease and rheumatoid arthritis. Based on these data investigators have approached us to be provided with seliciclib so that they can evaluate it in various indications in clinical trials.

In this regard, there are on-going investigator sponsored trials, or ISTs, evaluating seliciclib in endocrinologic and inflammatory indications in patients who have failed prior treatments. In an IST at Cedars-Sinai, Los Angeles, the first patients are being treated in an on-going Phase 2 trial to evaluate seliciclib as a potential therapy for Cushing's disease caused by pituitary tumors. There are limited options for Cushing's disease patients today. The investigator was awarded a grant from The National Institute of Diabetes and Digestive and Kidney Diseases. In a European IST, seliciclib is being evaluated as a potential treatment for rheumatoid arthritis, or RA, where it may work for RA by targeting proliferating fibroblasts, a different type of approach than conventional RA therapies. This study is also being supported by an approximately $1.5 million grant from the United Kingdom's Medical Research Council.

Collaboration and Licensing Agreement

On June 29, 2015, we announced the execution of a collaboration, licensing and supply agreement with ManRos Therapeutics SA, or ManRos, for the exclusive development and commercialization of our oral seliciclib capsules by ManRos as a treatment for cystic fibrosis, or CF. Among other terms of the agreement, ManRos licensed rights to our proprietary clinical data to enable clinical development of seliciclib for CF indications. The agreement provides for our supply of seliciclib investigational product for initial and later stage clinical trials of seliciclib in CF and technical assistance related to our know-how to facilitate these trials. We have received upfront payments and will receive milestone payments and tiered royalties if seliciclib is commercialized for the treatment of CF.

As with all ISTs and the collaboration and licensing agreement, we do not control the timing or conduct of such studies and will report updates as the investigators may notify us from time to time.

Recent Developments

Termination of Cantor Facility

Effective as of June 17, 2016, and prior to entering into the sales agreement with FBR, we and Cantor Fitzgerald & Co., or Cantor, agreed to terminate the Controlled Equity OfferingSM sales agreement, dated July 10, 2015, by and among us and Cantor. As previously reported, pursuant to the terms of the Cantor's sales agreement, we could offer and sell shares of our common stock having an aggregate offering price of up to $8.35 million from time to time through Cantor. We sold an aggregate of 114,077 shares pursuant to the Cantor's sales agreement.

Compliance with The NASDAQ Stock Market Continued Listing Requirements

On June 15, 2016, we received notification from the Listing Qualifications Staff of NASDAQ that we have regained compliance with the minimum bid price rule for continued listing on The NASDAQ Capital

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Market. The notification stated that as of June 14, 2016, we have evidenced a closing per share bid price of our common stock in excess of the $1.00 minimum closing bid price requirement for at least ten consecutive trading days. Accordingly, we have regained compliance with NASDAQ Listing Rule 5550(a)(2) and will continue to trade on The NASDAQ Capital Market.

Corporate Information

Our corporate headquarters are located at 200 Connell Drive, Suite 1500, Berkeley Heights, New Jersey, 07922, and our telephone number is (908) 517-7330. This is also where our medical and regulatory functions are located. Our research facility is located in Dundee, Scotland, which is also the center of our translational work and development programs. Our Internet address is http://www.cyclacel.com. The information on our website is not a part of, and should not be construed as being incorporated by reference into, this prospectus supplement or the accompanying prospectus.

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THE OFFERING

Common stock offered by us pursuant to this prospectus supplement

Shares of our common stock having an aggregate offering price of up to $4.0 million. In no event will we sell securities with a value exceeding more than one-third of our "public float" (the market value of our common stock and any other equity securities that we may issue in the future that are held by non-affiliates) in any 12-calendar month period.

Common stock to be outstanding after this offering

Up to 3,773,204 shares, assuming sales of 766,000 shares of our common stock in this offering at an offering price of $5.22 per share, which was the last reported sale price of our common stock on the NASDAQ Capital Market on June 22, 2016. The actual number of shares issued will vary depending on the sales price under this offering.

Manner of offering

"At the market offering" that may be made from time to time on the NASDAQ Capital Market or other market for our common stock in the United States through our agent, FBR Capital Markets & Co.. See the section entitled "Plan of Distribution" on page S-18 of this prospectus supplement.

Use of proceeds

We intend to use the net proceeds from this offering, if any, for our operations, for working capital and other general corporate purposes. See the section entitled "Use of Proceeds" on page S-16 of this prospectus supplement.

Risk factors

See the "Risk Factors" section in this prospectus supplement and the accompanying prospectus and the other information included in, or incorporated by reference into, this prospectus supplement for a discussion of certain factors you should carefully consider before deciding to invest in shares of our common stock.

NASDAQ Capital Market symbol

CYCC

The number of common stock to be outstanding immediately after this offering as shown above is based on 3,007,204 shares of common stock outstanding as of June 22, 2016, but exclude the following as of such date:

- 393,345 shares of common stock issuable upon the exercise of outstanding options at a weighted-average exercise price of $41.64 per share;

- 472 shares of common stock available for issuance under our 2015 Equity Incentive Plan;

- 45,343 shares of common stock issuable upon the exercise of outstanding warrants at a weighted-average exercise price of $114.24 per share; and

- 1,698 shares of common stock, subject to adjustment, that are issuable upon the conversion of 335,273 shares of convertible preferred stock that are issued and outstanding.

All references in this prospectus to number of shares of common stock, price per share and weighted average shares of common stock have been adjusted to reflect the Reverse Stock Split on a retroactive basis for all periods presented, unless otherwise noted.

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RISK FACTORS

Investing in our securities involves risk. Prior to making a decision about investing in our securities, you should carefully consider all of the information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus. In particular, you should carefully consider the risks, uncertainties and assumptions discussed under the heading "Risk Factors" in our most recent annual report on Form 10-K, which is on file with the SEC and incorporated by reference in this prospectus, and in subsequent filings that we make with the SEC. 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 and financial results.

Risks Associated with this Offering

Our management will have broad discretion over the use of any net proceeds from this offering, you may not agree with how we use the proceeds, and the proceeds may not be invested successfully.

Our management will have broad discretion as to the use of any net proceeds from this offering and could use them for purposes other than those contemplated at the time of this offering. Accordingly, you will be relying on the judgment of our management with regard to the use of any proceeds from the sale of shares of common stock in this offering, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. It is possible that the proceeds will be invested in a way that does not yield a favorable, or any, return for you.

You will experience immediate accretion.

The offering price per share in this offering may exceed the net tangible book value per share of our common stock outstanding prior to this offering. Assuming that an aggregate of 766,000 shares of our common stock are sold at a price of $5.22 per share, the last reported sale price of our common stock on June 22, 2016, for aggregate gross proceeds of $4.0 million, and after deducting commissions and estimated offering expenses payable by us, you will experience immediate accretion of $0.06 per share, representing the difference between our as adjusted net tangible book value per share as of March 31, 2016 after giving effect to this offering at the assumed offering price. The exercise of outstanding stock options and warrants will result in dilution of your investment. See the section entitled "Dilution" below for a more detailed illustration of the dilution you would incur if you participate in this offering.

Our shareholders may experience significant dilution as a result of future equity offerings or issuances and exercise of outstanding options and warrants.

In order to raise additional capital or pursue strategic transactions, we may in the future offer, issue or sell additional shares of common stock or other securities convertible into or exchangeable for shares of our common stock. We cannot assure you that we will be able to sell shares or other securities in any other transaction at a price per share or that have an exercise price or conversion price per shares that is equal to or greater than the price for the securities purchased by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing shareholders. The price per share at which we sell or issue additional shares of common stock or other securities convertible into or exchangeable for our common stock future transactions may be higher or lower than such price.

Sales of a significant number of shares of our common stock in the public markets, or the perception that such sales could occur, could depress the market price of our common stock.

Sales of a substantial number of shares of our common stock in the public markets could depress the market price of our common stock and impair our ability to raise capital through the sale of additional equity securities. We cannot predict the effect that future sales of our common stock would have on the market price of our common stock.

We do not intend to pay any cash dividends on our common stock in the foreseeable future and, therefore, any return on your investment in our common stock must come from increases in the fair market value and trading price of our common stock.

We do not intend to pay any cash dividends on our common stock in the foreseeable future and, therefore, any return on your investment in our common stock must come from increases in the fair market value and trading price of our common stock.

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The shares of common stock offered under this prospectus supplement and the accompanying prospectus may be sold in "at the market" offerings, and investors who buy shares at different times will likely pay different prices.

Investors who purchase shares under this prospectus supplement and the accompanying prospectus at different times will likely pay different prices, and so may experience different outcomes in their investment results. We will have discretion, subject to market demand, to vary the timing, prices, and numbers of shares sold, and there is no minimum or maximum sales price. Investors may experience declines in the value of their shares as a result of share sales made at prices lower than the prices they paid.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and the accompanying prospectus contain forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this prospectus supplement and the accompanying prospectus, including statements regarding our future results of operations and financial position, business strategy and plans and objectives of management for future operations, are forward-looking statements. The words “may,” “will,” “should,” “expects,” “plans,” “anticipates,” “could,” “intends,” “target,” “contemplates,” “believes,” “estimates,” “predicts,” “potential” or “continue” or the negative of these terms or other similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this prospectus supplement include, among other things, statements about:

- 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.

We may not actually 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. We have included important factors in the cautionary statements included in this prospectus supplement and the accompanying prospectus, particularly in the “Risk Factors” section, as well as the risk factors incorporated by reference in this prospectus supplement and the accompanying prospectus, discussed under “Risk Factors” in our Annual Report on Form 10-K for the fiscal year ended December 31, 2015, and under similar headings in our subsequently filed quarterly reports on Form 10-Q and annual reports on Form 10-K, that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this prospectus supplement, the accompanying prospectus and the documents that we have filed as exhibits to this prospectus supplement and the accompanying prospectus completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by applicable law.

This prospectus supplement and the accompanying prospectus include statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information.

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USE OF PROCEEDS

We may issue and sell shares of our common stock having aggregate sales proceeds of up to $4.0 million from time to time. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time.

We intend to use any net proceeds from the sale of common stock under this prospectus supplement and the accompanying prospectus for our operations, working capital and other general corporate purposes.

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 supplement for any purpose. Pending use of any net proceeds, we would expect to invest any proceeds in a variety of capital preservation instruments, including short-term, investment grade, interest bearing instruments.

DIVIDEND POLICY

We have never declared nor paid any cash dividends on our common stock and do not currently anticipate declaring or paying any cash dividends on our outstanding shares of common stock in the foreseeable future. We are, however, required to make or accrue quarterly dividend payments on our shares of convertible preferred stock. Except for dividends that may be paid on the shares of convertible preferred stock, we currently intend to retain all of our future earnings, if any, to finance operations. Any future determination relating to our dividend policy will be made at the discretion of our Board of Directors and will depend on a number of factors, including future earnings, capital requirements, financial conditions, future prospects, contractual restrictions and other factors that our Board of Directors may deem relevant.

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DILUTION

If you invest in our common stock, your interest will be diluted to the extent of the difference between the price per share you pay in this offering and the net tangible book value per share of our common stock immediately after this offering. Our net tangible book value of our common stock as of March 31, 2016, was approximately $15.9 million, or approximately $5.36 per share of common stock based upon 2,965,208 shares outstanding as of March 31, 2016. Net tangible book value per share is equal to our total tangible assets, less our total liabilities, divided by the total number of shares outstanding as of March 31, 2016.

After giving effect to the sale of our common stock in the aggregate amount of $4.0 million at an assumed offering price of $5.22 per share, the last reported sale price of our common stock on the NASDAQ Capital Market on June 22, 2016, and after deducting estimated offering commissions and expenses payable by us, our net tangible book value as of March 31, 2016 would have been $19.7 million, or $5.28 per share of common stock. This represents an immediate decrease in net tangible book value of $0.08 per share to our existing stockholders and an immediate accretion in net tangible book value of $0.06 per share to new investors in this offering.

The following table illustrates this calculation on a per share basis:

Assumed public offering price per share		$ 5.22
Historical net tangible book value per share as of March 31, 2016	$ 5.36	
Decrease in net tangible book value per share attributable to this offering	$ (0.08)	
As adjusted net tangible book value per share after giving effect to this offering		$ 5.28
Accretion in net tangible book value per share to new investors in this offering		$ 0.06

The number of shares of our common stock to be outstanding immediately after this offering is based on 2,965,208 shares of our common stock outstanding as of March 31, 2016. The number of shares outstanding as of March 31, 2016 excludes:

- 376,775 shares of common stock issuable upon the exercise of outstanding options at a weighted-average exercise price of $41.64 per share;
- 17,574 shares of common stock available for issuance under our 2015 Equity Incentive Plan;
- 45,343 shares of common stock issuable upon the exercise of outstanding warrants at a weighted-average exercise price of $114.24 per share;
- 1,698 shares of common stock, subject to adjustment, that are issuable upon the conversion of 335,273 shares of convertible preferred stock that are issued and outstanding; and
- 41,996 shares of common stock issued after March 31, 2016.

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PLAN OF DISTRIBUTION

We have entered into a sales agreement with FBR under which we may offer and sell shares of our common stock from time to time through FBR, acting as agent. Sales of shares of our common stock, if any, under this prospectus supplement and the accompanying prospectus may be made in negotiated transactions or transactions that are deemed to be "at the market offerings" as defined in Rule 415 under the Securities Act, including, without limitation, including sales made directly on or through the NASDAQ Capital Market, the existing trading market for our common stock, sales made to or through a market maker other than on an exchange or otherwise, in negotiated transactions at market prices, and/or any other method permitted by law.

FBR will offer our common stock subject to the terms and conditions of the sales agreement as agreed upon by us and FBR. We will designate the number of shares which we desire to sell, the time period during which sales are requested to be made, any limitation on the number of shares that may be sold in one day and any minimum price below which sales may not be made. Subject to the terms and conditions of the sales agreement, FBR will use their commercially reasonable efforts to sell on our behalf all of the shares of common stock requested to be sold by us. FBR or we may suspend the offering of our common stock being made under the sales agreement upon proper notice to the other party.

We will pay commissions to FBR for its services in acting as agent in the sale of our common stock at a commission rate equal to 3.0% of the gross sale price per share sold. We estimate that the total expenses for this offering, excluding commissions payable under the sales agreement, will be approximately $205,000. We have agreed to reimburse FBR for its reasonable out-of-pocket expenses, including attorneys' fees, in an amount not to exceed $35,000 in the aggregate, which amount is included in the estimated total expenses for this offering.

Settlement for sales of common stock will occur on the third business day following the date on which any sales are made, or on another date that is agreed upon by us and FBR in connection with a particular transaction, in return for payment of the net proceeds to us. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

In connection with the sale of the common stock on our behalf, FBR may be deemed to be an underwriter within the meaning of the Securities Act, and the compensation may be deemed to be underwriting commissions or discounts. We have agreed to provide indemnification and contribution to FBR against certain civil liabilities, including liabilities under the Securities Act.

This offering will terminate upon the earlier of (1) the issuance and sale of all shares of our common stock covered by this prospectus supplement and (2) the termination of the sales agreement as permitted therein.

FBR and each of its affiliates may in the future provide various investment banking and other financial services for us and our affiliates, for which services they may in the future receive customary fees. To the extent required by Regulation M, FBR will not engage in any market making activities involving our common stock while the offering is ongoing under this prospectus supplement.

This summary of the material provisions of the sales agreement does not purport to be a complete statement of its terms and conditions. A copy of the sales agreement has been filed with the SEC on a Current Report on Form 8-K.

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LEGAL MATTERS

Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., New York, New York, will pass upon the validity of the issuance of the securities to be offered by this prospectus supplement. Duane Morris LLP, Newark, New Jersey, is counsel for FBR in connection with this offering.

EXPERTS

The consolidated financial statements of Cyclacel Pharmaceuticals, Inc., appearing in our Annual Report on Form 10-K for the fiscal years ended December 31, 2015 and 2014, have been audited by RSM US LLP, independent registered public accounting firm, as set forth in their report thereon, 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.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, and file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy these reports, proxy statements and other information at the SEC's public reference facilities at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference facilities. SEC filings are also available at the SEC's web site at http://www.sec.gov.

This prospectus supplement is only part of a registration statement on Form S-3 that we have filed with the SEC under the Securities Act and therefore omits certain information contained in the registration statement. We have also filed exhibits and schedules with the registration statement that are excluded from this prospectus supplement, and you should refer to the applicable exhibit or schedule for a complete description of any statement referring to any contract or other document. You may inspect a copy of the registration statement, including the exhibits and schedules, without charge, at the public reference room or obtain a copy from the SEC upon payment of the fees prescribed by the SEC. We also maintain a website at http://www.cyclacel.com, through which you can access our SEC filings. The information set forth on, or accessible from, our website is not part of this prospectus supplement or the accompanying prospectus.

INCORPORATION OF DOCUMENTS BY REFERENCE

The SEC allows us to "incorporate by reference" information that we file with them. Incorporation by reference allows us to disclose important information to you by referring you to those other documents. The information incorporated by reference is an important part of this prospectus supplement, and information that we file later with the SEC will automatically update and supersede this information. This prospectus supplement omits certain information contained in the registration statement, as permitted by the SEC. You should refer to the registration statement and any prospectus supplement filed hereafter, including the exhibits, for further information about us and the securities we may offer pursuant to this prospectus supplement. Statements in this prospectus supplement regarding the provisions of certain documents filed with, or incorporated by reference in, the registration statement are not necessarily complete and each statement is qualified in all respects by that reference. Copies of all or any part of the registration statement, including the documents incorporated by reference or the exhibits, may be obtained upon payment of the prescribed rates at the offices of the SEC listed above in "Where You Can Find More Information." The documents we are incorporating by reference are:

- Our Annual Report on Form 10-K for the year ended December 31, 2015, filed on March 29, 2016;

- Our Quarterly Report on Form10-Q for the quarter ended March 31, 2016, filed on May 13, 2016;

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- Our Current Reports on Form 8-K filed on February 5, 2016, March 24, 2016, April 11, 2016, May 11, 2016, May 27, 2016 and June 23, 2016 (except for the information furnished under Items 2.02 or 7.01 and the exhibits furnished thereto);

- Our definitive Proxy Statement relating to our 2016 annual meeting of stockholders filed on April 11, 2016;

- 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.

- 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; and

- all reports and other documents subsequently filed by us pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Exchange Act after the date of this prospectus supplement and prior to the termination or completion of the offering of securities under this prospectus supplement shall be deemed to be incorporated by reference in this prospectus supplement and to be a part hereof from the date of filing such reports and other documents.

Unless otherwise noted, the SEC file number for each of the documents listed above is 000-50626.

In addition, all reports and other documents filed by us pursuant to the Exchange Act after the date of the initial registration statement and prior to effectiveness of the registration statement shall be deemed to be incorporated by reference into this prospectus supplement.

Any statement contained in this prospectus supplement or in a document incorporated or deemed to be incorporated by reference into this prospectus supplement will be deemed to be modified or superseded for purposes of this prospectus supplement to the extent that a statement contained in this prospectus supplement or any other subsequently filed document that is deemed to be incorporated by reference into this prospectus supplement modifies or supersedes the statement. Any statement so modified or superseded will not be deemed, except as so modified or superseded, to constitute a part of this prospectus supplement.

You may request, orally or in writing, a copy of these filings, which will be provided to you at no cost, by writing or calling us at: 200 Connell Drive, Suite 1500, Berkeley Heights, NJ 07922, telephone (908) 517-7330. Information about us is also available at our website at http://www.cyclacel.com. However, the information in our website is not a part of this prospectus and is not incorporated by reference into this prospectus.

You should rely only on information contained in, or incorporated by reference into, this prospectus supplement and any prospectus supplement. We have not authorized anyone to provide you with information different from that contained in this prospectus supplement or incorporated by reference in this prospectus supplement. We are not making offers to sell the securities in any jurisdiction in which such an offer or solicitation is not authorized or in which the person making such offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make such offer or solicitation.

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PROSPECTUS

$100,000,000

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 $100,000,000 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 describes 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 may 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.

On May 27, 2016, we implemented a one-for-twelve reverse stock split of our issued and outstanding shares of common stock (the "Reverse Stock Split"). The Reverse Stock Split became effective at the opening of trading on The NASDAQ Capital Market on May 31, 2016. All references in this prospectus to number of shares of common stock, price per share and weighted average shares of common stock have been adjusted to reflect the Reverse Stock Split on a retroactive basis for all periods presented, unless otherwise noted.

Our common stock is listed on The NASDAQ Capital Market under the symbol "CYCC," and our preferred stock is listed on The NASDAQ Capital Market under the symbol "CYCCP." On June 8, 2016, the last reported sale price of our common stock was $6.00 per share, and the last reported sale price of our preferred stock was $6.97 per share.

The aggregate market value of our outstanding shares of common stock held by non-affiliates was $16,539,985.40 based on 3,079,285 shares of common stock outstanding, as of the date of this prospectus, of which 2,572,315 shares were held by non-affiliates, and a per share price of $6.43 based on the closing sale price of our common stock on the NASDAQ Capital Market on June 6, 2016 (after giving effect to the Reverse Stock Split). Pursuant to General Instruction I.B.6 of Form S-3, in no event will we sell securities pursuant to this prospectus with a value of more than one-third of the aggregate market value of our common stock held by non-affiliates in any twelve-month period, so long as the aggregate market value of our common stock held by non-affiliates is less than $75,000,000. In the event that subsequent to the date of this prospectus, the aggregate market value of our outstanding common stock held by non-affiliates equals or exceeds $75,000,000, then the one-third limitation on sales shall not apply to additional sales made pursuant to this prospectus. During the prior twelve calendar months prior to, and including, the date of this prospectus, we sold $1,101,984 of securities pursuant to General Instruction I.B.6 of Form S-3.

The applicable prospectus supplement will contain information, where applicable, as to any other listing, if any, on The NASDAQ Capital 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 14 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 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 June 8, 2016.

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

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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 $100,000,000. 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, 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 14 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

General

We are a biopharmaceutical company dedicated to the development and commercialization of novel, mechanism-targeted drugs to treat human cancers and other serious diseases. Our strategy is to build a diversified biopharmaceutical business in hematology and oncology based on a development pipeline of novel drug candidates.

Drug Candidates

The cell cycle, the biological process by which cells propagate 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, replicates its DNA and divides. This process also includes mechanisms to ensure errors are corrected, and if not, the cells commit suicide or apoptose. 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, seliciclib and CYC065. 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.

Our lead candidate, sapacitabine, is a novel, orally-available nucleoside analog. A number of nucleoside drugs, such as gemcitabine and cytarabine, also known as Ara-C, both generic drugs, 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 fluorouracil, or 5-FU, two widely used nucleoside analogs, in delaying the onset and growth of liver metastasis. We hold the 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.

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 a Phase 2 study for MDS and in a Phase 1/2 study in solid tumors in combination with seliciclib, another of our drug candidates. Sapacitabine has been evaluated in approximately 1,000 patients to date.

In our second development program, we are evaluating cyclin dependent kinase, or CDK, inhibitors. CDKs are involved in cancer cell growth, survival, metastatic spread and DNA damage repair. Seliciclib, our lead CDK inhibitor, is an oral, highly selective inhibitor of CDK2/9 enzymes that are central to the

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process of cell division and cell cycle control. To date, seliciclib has been evaluated in over 450 patients with various cancers, including non-small cell lung cancer, or NSCLC, and nasopharyngeal cancer, or NPC, and has shown signs of anticancer 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. Seliciclib is also being evaluated in Investigator Sponsored Trials, or ISTs, to treat Cushing's disease and rheumatoid arthritis, and in a license and supply agreement for the treatment of cystic fibrosis.

Our second generation CDK inhibitor, CYC065, is a highly selective inhibitor of CDKs targeting CDK2/9 enzymes with potential utility in both hematological malignancies and solid tumors. CYC065 has increased anti-proliferative potency and improved pharmaceutical properties compared to seliciclib. CYC065 is in an on-going first-in-human, Phase 1 trial to assess its safety, tolerability, pharmacokinetics and pharmacodynamics in advanced cancer patients. CYC065 was selected from the Company's discovery program in Dundee, Scotland and its development was supported in part by a $1.9 million grant from the Biomedical Catalyst of the United Kingdom government.

In addition to these development programs, in our polo-like kinase, or PLK, inhibitor program, we have discovered CYC140 and other potent and selective small molecule inhibitors of PLK1, a kinase that is active during cell division and which targets the mitotic phase of the cell cycle. PLK was discovered by Professor David Glover, our Chief Scientist. We have received a grant award of approximately $3.5 million from the Biomedical Catalyst of the United Kingdom government to complete IND-directed preclinical development of CYC140.

We currently retain virtually all marketing rights worldwide to the compounds associated with our drug programs. To optimize our commercial return, we intend to enter into selected partnering arrangements.

Clinical 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 analogs, CDK inhibitors, PLK inhibitors and Aurora Kinase/vascular endothelial growth factor receptor, or AK/VEGFR inhibitors. 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 biological substances or effects whose presence in patient samples can serve as an indicator or marker of diseases, or may highlight patients more likely to respond to a particular treatment. Biomarker data from early clinical trials may also enable us to design subsequent trials more efficiently and to monitor patient compliance with trial protocols. For example, we reported that sapacitabine efficacy is enhanced in tumor cells that are defective in homologous recombination DNA repair and that sapacitabine treatment increased a DNA damage marker in patient samples. We believe that in the longer term biomarkers may allow the selection of patients more likely to respond to our drugs in clinical trials and increase the benefit to patients.

Although a number of pharmaceutical and biotechnology companies are currently attempting to develop nucleoside analogs, CDK inhibitors 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 analog presently being tested in a Phase 3 trial in previously untreated AML and in Phase 2 for high risk MDS.

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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. Enrollment completed	DNA polymerase	G2 and S phase
Sapacitabine, CYC682	MDS	Phase 2 randomized trial Enrollment completed	DNA polymerase	G2 and S phase
Seliciclib + Sapacitabine	Cancer	Phase 1/2 trial on-going		
CYC065 CDK inhibitor	Cancer	Phase 1 first-in-human solid tumors and lymphoma; on-going	CDK2/9	G1/S checkpoint and others
CYC140 PLK inhibitor	Cancer	Preclinical	PLK1	G2/M checkpoint
Investigator Sponsored Trials				
Seliciclib, CYC202	Cushing's disease and rheumatoid arthritis	Phase 2 trial	CDK2/9	G1/S checkpoint and others
Licensing & Collaboration				
Seliciclib, CYC202	Cancer	Phase 2 trial		

Market opportunity in hematology

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.

AML is a cancer of the blood cells that progresses rapidly and if not treated, could be fatal within a few months. AML is generally a disease of older people and is uncommon before the age of 40. The average age of a patient with AML is about 67 years. According to The Surveillance, Epidemiology, and End Results, or SEER, program of the National Cancer Institute, or NCI, the incidence rate of AML is approximately 20,000 in the United States. It is estimated that European incidence is approximately 22,000. A review of The University of Texas MD Anderson Cancer Center's historical experience with front-line intensive induction chemotherapy for AML patients aged 70 years or older demonstrated that while 45% achieved a complete remission, median overall survival was only 4.6 months and was associated with a 4-week death rate of 26% and an 8-week death rate of 36%.

MDS is a family of clonal myeloid neoplasms, or malignancies of the blood, caused by the failure of blood cells in the bone marrow to develop into mature cells. Patients with MDS typically suffer from bone marrow failure and cytopenias, or reduced counts of platelets, red and white blood cells. The exact incidence and prevalence of MDS are unknown because it can go undiagnosed and a national survey canvassing both hospitals and office practitioners has not been completed. Some estimates place MDS incidence at 15,000 to 20,000 new cases each year in the United States alone with some authors estimating incidence as high as 46,000. Literature suggests that there is a rising incidence of MDS as the age of the population increases with the majority of patients aged above 60 years. Patients currently receive hypomethylating agents as first-line treatment. There is no approved therapy for second-line treatment.

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Sapacitabine

Sapacitabine, previously known as CYC682, is an orally-available nucleoside analog. 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 beta-elimination reaction and leading to the formation of single-strand DNA breaks, or SSBs. During subsequent rounds of replication, SSBs are converted to double-strand breaks, or DSBs; these can be repaired by the homologous recombination repair, or HRR, pathway, or, if unrepaired, result in cell death.

We are currently exploring sapacitabine in both hematological cancers and solid tumors. Approximately 1,000 patients have received sapacitabine in Phase 1, 2 and 3 studies.

Hematological Cancers

SEAMLESS, randomized Phase 3, pivotal trial of sapacitabine in elderly patients with AML

The SEAMLESS study is being conducted under an SPA agreement that Cyclacel reached with the FDA.

The study is chaired by Hagop M. Kantarjian, M.D., Chairman and Professor, Department of Leukemia, The University of Texas MD Anderson Cancer Center. SEAMLESS is a multicenter, randomized, Phase 3 study of sapacitabine as a front-line treatment in approximately 485 elderly patients aged 70 years or older with newly diagnosed AML who are not candidates for or have refused intensive induction chemotherapy. In SEAMLESS an investigational arm of oral sapacitabine administered in alternating cycles with intravenous decitabine is compared with a control arm of intravenous decitabine administered alone. The primary efficacy endpoint is overall survival.

SEAMLESS completed enrollment in December 2014 with approximately 110 centers participating from the United States and Europe. Also in December 2014, the Data Safety Monitoring Board, or DSMB, conducted a planned interim analysis for futility after 247 events, or patient deaths, and the final safety review of 470 randomized patients. The DSMB found no safety concerns. However, the planned futility boundary has been crossed and the DSMB determined that, based on available interim data, it would be unlikely for the study to reach statistically significant improvement in survival. The DSMB saw no reasons why patients should discontinue treatment on their assigned arm and recommended that recruited patients stay on treatment.

The interim analysis for futility performed in December 2014 was primarily driven by the events within the first 6 months of patients entering into the trial. Of 247 events in SEAMLESS, 173 (70%) have occurred in the first 6 months. This means that the survival curves beyond 6 months are poorly estimated at the time of the analysis. Furthermore, follow up of European patients at December 2014 is significantly shorter than that of U.S. patients as the study opened for European accrual in April 2014. It is important to have complete follow up of all patients to ensure that a potential treatment effect beyond 6 months is not missed.

In accordance with the DSMB’s recommendations, we continue to follow-up patients as per the study protocol until the prespecified 424 events have been observed. This is estimated to occur in the first half of 2016. Approximately 4% of the prespecified events remain to be observed as of March 25, 2016.

In parallel to the follow-up of enrolled patients we have submitted, and have received validation of, a Pediatric Investigation Plan, or PIP, to the EMA. The EMA requires sponsors to agree to a PIP before a marketing authorization application, or MAA, can be accepted, and because the lead times can be long, we submitted the PIP ahead of any MAA submission. Depending on the final data, we may meet with regulatory authorities in Europe and the United States to discuss registration submissions for sapacitabine for the AML indication.

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Pilot/Lead-in study of sapacitabine in elderly patients with AML

Results from a single-arm, multicenter, Phase 1/2 clinical trial examining the safety and efficacy of oral sapacitabine administered sequentially with intravenous decitabine, the same regimen as in the investigational arm of SEAMLESS, were reported during a poster session at the 2012 American Society of Hematology, or ASH, Annual Meeting. 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 one-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 study of sapacitabine in patients with previously untreated or first relapse AML

SEAMLESS builds on promising one year survival observed in elderly patients with AML enrolled in a Phase 2 study of single agent sapacitabine. In December 2007, we initiated a multicenter, randomized Phase 2 clinical trial of oral sapacitabine in 60 elderly patients with AML aged 70 years or older who were previously untreated or in first relapse. The Phase 2 study, led by Dr. Kantarjian, had a primary endpoint of one year survival and randomized patients to one of three dosing schedules of sapacitabine. Secondary objectives were to assess complete remission, or CR, partial remission, or PR, duration of CR or CRp, or major hematological improvement and their corresponding durations, transfusion requirements, number of hospitalized days and safety. The study used 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 would produce a better one year survival rate in the event that all three dosing schedules were 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. Between December 27, 2007 and April 21, 2009, a total of 105 patients were enrolled and treated in the Phase 2 study. Their median age was 77 years with a range of 70-91 years. 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 was assigned to one of three dosing schedules: 200 mg twice a day for 7 days (Arm A); 300 mg twice a day for 7 days (Arm B); and 400 mg twice a day for 3 days each week for 2 weeks (Arm C). All schedules were given in 28 day cycles. The 3-day dosing schedule in Arm 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 one-year survival rate of 30%, median overall survival of 213 days and durable complete remissions, or CRs, in 25% of patients. The median overall survival of patients from all arms 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.

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

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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, or 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 one-year survival with the objective of identifying a dosing schedule that produces a better one-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 December 2013 at the 2013 ASH Meeting and Exposition, we announced primary endpoint data from the ongoing, open-label, multicenter, randomized Phase 2 trial of oral sapacitabine capsules in older patients with myelodysplastic syndromes after treatment failure of front-line hypomethylating agents, such as azacitidine and/or decitabine. The median overall survival for each arm was approximately 9.7 months for Arm G, 9.7 months for Arm H, and 7.6 months for Arm I. The median overall survival for all three arms was approximately 8.6 months. One-year survival was 38% for Arm G, 24% for Arm H, and 33% for Arm I. Nine patients had responded (2 CRs, 2 CRp, and 5 major HIs): 19% for Arm G, 10% for Arm H and 14% for Arm I and the time to response was one to four cycles. Median number of cycles was three with a range of one to over 23 and 30 patients received four or more cycles. Additionally, 23 patients achieved stable disease lasting longer than 16 weeks. The 30 day mortality from all causes was 5% in each of the three arms and ten patients, or approximately 16%, were still alive.

We have recently completed enrollment of a patient cohort in an additional part of the MDS Phase 2 study in order to evaluate better dosing regimens. We will follow-up these additional Phase 2 patients until mature survival data become available. In parallel, we anticipate initiating a Phase 1/2 trial of sapacitabine in combination with other agents to determine safety and tolerability. We would expect to plan a Phase 2 randomized controlled trial, or RCT, of sapacitabine in combination with other agents following a review of all relevant clinical data with mature follow-up. Median overall survival after treatment failure of front-line hypomethylating agents, such as azacitidine and/or decitabine, for patients with intermediate-2 or high- risk disease per IPSS, is reported in the literature to range between 5.9 and 4.3 months. Patients with high-risk 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.

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

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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.

Cyclin Dependent Kinase Inhibitor program

Cyclin Dependent Kinase Inhibitors, or CDKs, are enzymes that are central to the process of cell division and cell cycle control and play pivotal roles in cancer cell growth, survival and DNA damage repair. Inhibition of CDKs 2 and 9 may also overcome aberrant cell cycle control in certain non-malignant diseases of proliferation.

Seliciclib

Seliciclib, is a novel, orally-available, CDK2/7/9 inhibitor which has a target profile 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 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 over 450 patients in several Phase 1 and 2 studies, including studies in NSCLC and NPC, and has shown signs of anti-cancer activity. We have retained worldwide rights to commercialize seliciclib.

Phase 1/2 clinical trial of seliciclib and sapacitabine in patients with advanced cancers

In an ongoing Phase 1, single-arm, dose escalation study, sapacitabine and seliciclib are administered sequentially in patients with incurable advanced solid tumors unresponsive to conventional treatment or for which no effective therapy exists. Sapacitabine is dosed twice daily for 7 days (Day 1-7) and seliciclib twice daily for 3 days (Day 8-11) for three week cycles. 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 is to evaluate the antitumor activity of sequential treatment and to explore the pharmacodynamic effect of this treatment in skin and peripheral blood mononuclear cells. The study is being conducted at Dana Farber Cancer Institute in Boston and the principal investigator is Geoffrey I. Shapiro, MD with participation from other Harvard Medical School hospitals.

At the 2013 American Society of Cancer Research Annual Meeting Dr Shapiro reported that of 38 patients with incurable solid tumors and adequate organ function enrolled in the Phase 1 study, 16 were BRCA mutation positive. Four patients with BRCA-deficient pancreatic, breast or ovarian cancers had confirmed partial responses to the drug regimen. Based on available follow-up to date, three patients experienced durable partial responses, with a breast cancer patient receiving treatment over 234 weeks or 78 three-week cycles which is on-going. Researchers observed stable disease of 12 weeks or more in eight additional patients, including two BRCA positive patients with ovarian and breast cancers and whose stable disease lasted 64 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.

As of December 2015, approximately 60 patients with various cancers have been enrolled, of which approximately two-thirds are BRCA positive.

Based on encouraging results from the initial patients and investigator interest the study has been expanded to evaluate an additional 20 breast cancer patients all of whom are required to test positive for BRCA in baseline biopsies. Patients will also undergo whole exome sequencing with the objective of further characterizing the genetic profiles of their tumors.

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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.

CYC065

CYC065 is a highly-selective, second generation inhibitor of CDK2 and CDK9 that causes apoptotic death of cancer cells at sub-micromolar concentrations and is bioavailable via oral and intravenous routes. Antitumor efficacy has been achieved in vivo with once a day oral dosing at well tolerated doses. Evidence from published preclinical studies show that CYC065 may benefit patients with adult and pediatric hematological malignancies, including certain AML, Acute Lymphocytic Leukemias, or ALL, Chronic Lymphocytic Leukemias, or CLL, Diffuse Large B-cell Lymphoma, or DLBCL, Multiple Myelomas or MM, and certain solid tumors, including breast and uterine cancers.

CYC065 is in an on-going, first-in-human, Phase 1 trial to assess its safety, tolerability, pharmacokinetics and pharmacodynamics in solid tumor and lymphoma patients. The trial is being conducted at the Dana Farber Cancer Institute in Boston and the principal investigator Dr Geoffrey I. Shapiro, M.D. CYC065 was selected from the Company's drug discovery program in Dundee, Scotland and its development was supported in part by a grant award of approximately $1.9 million from the Biomedical Catalyst of the United Kingdom government.

CYC065 is mechanistically similar but has much higher dose potency, in vitro and in vivo, improved metabolic stability and longer patent protection than seliciclib, Cyclacel's first generation CDK2/9 inhibitor. Translational biology data support development of CYC065 as a stratified medicine for solid and liquid tumors. CYC065 has been shown to reverse drug resistance associated with the addiction of cancer cells to cyclin E, a partner protein of CDK2, and inhibit CDK9-dependent oncogenic and leukemogenic pathways, including MYC and multilineage leukemia rearrangements, or MLL-r. Like seliciclib, CYC065 also represses the MCL-1-mediated survival pathway in cancer cells, leading to rapid induction of apoptosis in MCL-1 dependent cancer cells.

In 2011, independent investigators published preclinical evidence that CYC065 as a single-agent can induce tumor growth delay in HER2-positive breast cancer cells addicted to cyclin E and resistant to trastuzumab, or Herceptin®, while administration of CYC065 in combination with trastuzumab resulted in regression or sustained tumor growth inhibition.

Data presented at the American Association for Cancer Research, or AACR, 2016 Annual Meeting demonstrated the therapeutic potential of CYC065 as a targeted anti-cancer agent. The preclinical data shows that CYC065 can induce cell death, and that it combined beneficially with anti-cancer drugs from the Bcl-2 and BET inhibitor classes, in in vitro models of B-cell lymphoma, including double-hit lymphomas. The preclinical study evaluated both single-agent activity of CYC065 and combinations of CYC065 with the Bcl-2 inhibitor, venetoclax (ABT-199, Venclexta®), and BET (Bromodomain and Extra-Terminal) inhibitors in B-cell lymphoma cell lines. Short exposure to CYC065 was sufficient to downregulate MYC, an oncogene aberrantly expressed in many cancers, and Mcl-1, an anti-apoptotic member of the Bcl-2 family, and to induce cell death. CYC065 treatment had no impact on Bcl-2 levels. Combinations of CYC065 with venetoclax or BET inhibitors were both synergistic. CYC065 targets key oncogenic and survival pathways in double-hit B-cell lymphomas suggesting a therapeutic rationale for this indication.

Additionally, data presented at the 2015 Annual Meeting of the American Association of Cancer Research, or AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics demonstrated the mechanistic rationale for clinical development of CYC065 in oncology. Data showed that MLL gene status and levels of Bcl-2 family proteins correlated with sensitivity of AML cell lines to CYC065. Combination studies revealed the potential to combine CYC065 with available and experimental leukemia therapies, including cytarabine and Bcl-2 inhibitors. Potent anticancer activity of

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CYC065 was demonstrated in vivo in AML xenograft models resulting in over 90% inhibition of tumor growth. The potent in vitro and in vivo anti-cancer activity, opportunity for patient stratification and the ability to combine with anti-leukemic agents suggest that CYC065 may have therapeutic potential in AML.

Data presented at the 2015 San Antonio Breast Cancer Symposium demonstrated in particular the mechanistic rationale for clinical development of CYC065 in basal-like triple negative breast cancer, or TNBC, a cancer with poor prognosis frequently associated with BRCA mutations. Molecular characteristics of TNBC include amplification or overexpression of Cyclin E, the partner protein of CDK2, and MYC. CYC065 directs a pro-apoptotic mechanism in breast cancer cell lines, which includes transcriptional down regulation of key pro-survival and oncogenic regulators, including MCL-1 and MYC.

CYC065 was shown to rapidly induce cell death in breast cancer cell lines, while transiently inducing G1 cell cycle arrest in non-malignant breast lines. CYC065's potent anticancer activity has been confirmed in breast cancer xenograft animal models. Like seliciclib, CYC065 effectively combined with sapacitabine in breast cancer cell lines.

In 2015, independent investigators presented data demonstrating that CYC065 prolongs survival in MYCN-addicted neuroblastoma models. The study evaluated the ability of CYC065 to inhibit cell proliferation and induce apoptosis of neuroblastoma cells in vitro and in vivo. In vivo efficacy was evaluated in subcutaneous xenograft models of both MYCN-amplified and non-amplified neuroblastoma cells and the Th-MYCN genetically-engineered mouse model of neuroblastoma. The study showed that neuroblastoma cell lines with MYCN amplification and high MYCN expression levels were sensitive to the CYC065 inhibitor. CYC065 also depleted MYCN protein in a time- and dose-dependent manner, blocked neuroblastoma cell proliferation and induced apoptosis which resulted in significantly reduced tumor burdens and prolonged survival in MYCN-addicted neuroblastoma models in vivo.

Similar to palbociclib, a drug which targets CDK4/6 and the first CDK inhibitor to be recently approved by the FDA, we anticipate that CYC065 will likely be best used in combination with available anti-cancer agents. Depending on the data from the ongoing Phase 1 study, we are also interested in evaluating CYC065 in patients with hematological malignancies in light of profound signals of activity observed in preclinical studies.

PLK inhibitors

In our PLK inhibitor program we have discovered potent and selective small molecule inhibitors of PLK1, a kinase active during cell division, which target the mitotic phase of the cell cycle. At the 2012 Annual Meeting of the AACR, we reported that one of these compounds, CYC140, was selected for further preclinical development and showed potent activity and selectivity against a panel of esophageal cancer cell lines. 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. PLK was discovered by Professor David Glover, our Chief Scientist. We have received a grant award of approximately $3.5 million from the Biomedical Catalyst of the United Kingdom government to complete IND-directed preclinical development of CYC140.

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. Vascular endothelial growth factor receptor 2, or VEGFR2 is a receptor protein that plays a key regulatory role in the angiogenesis pathway, or blood vessel formation. VEGFR is targeted by 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 tested the activity of CYC3, our novel Aurora Kinase A specific inhibitor, in pancreatic cancer cell lines and found that CYC3 acted synergistically against pancreatic cancer cell lines in combination with paclitaxel at a 10-fold lower dose

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resulting in comparable anti-proliferative activity to standard paclitaxel dosing. The collaborators reported that the combination merits further investigation and has the potential for improved therapeutic index in vivo. We have 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, but have no current plans to progress the program. We have retained worldwide rights to commercialize CYC116 and our other Aurora kinase inhibitors.

Investigator-Sponsored Trials

Preclinical results from several independent investigators suggest that cell cycle inhibitors, such as seliciclib and related 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 glomerulonephritis, graft-versus-host disease, idiopathic pulmonary fibrosis, lupus nephritis, polycystic kidney disease and rheumatoid arthritis. Based on these data investigators have approached us to be provided with seliciclib so that they can evaluate it in various indications in clinical trials.

In this regard, there are on-going investigator sponsored trials, or ISTs, evaluating seliciclib in endocrinologic and inflammatory indications in patients who have failed prior treatments. In an IST at Cedars-Sinai, Los Angeles, the first patients are being treated in an on-going Phase 2 trial to evaluate seliciclib as a potential therapy for Cushing's disease caused by pituitary tumors. There are limited options for Cushing's disease patients today. The investigator was awarded a grant from The National Institute of Diabetes and Digestive and Kidney Diseases. In a European IST, seliciclib is being evaluated as a potential treatment for rheumatoid arthritis, or RA, where it may work for RA by targeting proliferating fibroblasts, a different type of approach than conventional RA therapies. This study is also being supported by an approximately $1.5 million grant from the United Kingdom's Medical Research Council.

Collaboration and Licensing Agreement

On June 29, 2015, we announced the execution of a collaboration, licensing and supply agreement with ManRos Therapeutics SA, or ManRos, for the exclusive development and commercialization of our oral seliciclib capsules by ManRos as a treatment for cystic fibrosis, or CF. Among other terms of the agreement, ManRos licensed rights to our proprietary clinical data to enable clinical development of seliciclib for CF indications. The agreement provides for our supply of seliciclib investigational product for initial and later stage clinical trials of seliciclib in CF and technical assistance related to our know-how to facilitate these trials. We have received upfront payments and will receive milestone payments and tiered royalties if seliciclib is commercialized for the treatment of CF.

As with all ISTs and the collaboration and licensing agreement, we do not control the timing or conduct of such studies and will report updates as the investigators may notify us from time to time.

Recent Developments

Deficiency and Compliance Notices from The NASDAQ Stock Market and Reverse Stock Split

As previously disclosed, on February 2, 2016, we received a letter from NASDAQ's Listing Qualifications Staff notifying us that, because we had not regained compliance with the $1.00 minimum bid price requirement for continued listing as set forth in NASDAQ Listing Rule 5550(a)(2) (the "Rule"), our common stock would be subject to delisting from NASDAQ unless the Company timely requested a hearing before a NASDAQ Listing Qualifications Panel (the "Panel"). We requested a hearing before the Panel, at which we presented a plan to regain compliance with the Rule and requested that the Panel allow us additional time to implement the plan. On April 4, 2016, the Panel rendered its written decision granting the Company until June 14, 2016 to regain compliance with the Rule.

As previously disclosed, in order to increase the per share trading price of the Company' common stock to satisfy the $1.00 minimum bid price requirement for continued listing on The NASDAQ Capital Market, on May 26, 2016, the Company filed a certificate of amendment to its amended and restated certificate of incorporation with the Secretary of State of the State of Delaware to effect a one-for-twelve

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reverse stock split of the Company's shares of common stock. As a result of the reverse stock split, every twelve shares of the Company's pre-reverse split common stock was combined and reclassified into one share of common stock (the "Reverse Stock Split"). The Reverse Stock Split became effective at 5:00 p.m., Eastern Time, on May 27, 2016, and the Company's common stock began trading on the NASDAQ Capital Market on a post-split basis at the open of business on May 31, 2016. With the implementation of the Reverse Stock Split, the Company expects to regain compliance with the Rule.

All references in this prospectus to number of shares of common stock, price per share and weighted average shares of common stock have been adjusted to reflect the Reverse Stock Split on a retroactive basis for all periods presented, unless otherwise noted.

Equity Transactions

Since last reported in our Annual Report on Form 10-K for the year ended December 31, 2015, we have raised net proceeds of $225,126 under a Controlled Equity OfferingSM sales agreement with Cantor Fitzgerald & Co.

Corporate Information

Our corporate headquarters are located at 200 Connell Drive, Suite 1500, Berkeley Heights, New Jersey, 07922, and our telephone number is (908) 517-7330. This is also where our medical and regulatory functions are located. Our research facility is located in Dundee, Scotland, which is also the center of our translational work and development programs.

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 $100,000,000, 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:

- 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.

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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 si substance used in connection 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.

Please also see the discussion of risks and uncertainties under the heading “Risk Factors” beginning on page 14.
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

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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.

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

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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 which 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 Capital Market. The applicable prospectus supplement will contain information, where applicable, as to any other listing, if any, on The NASDAQ Capital 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 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 so indicated 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 June 2, 2016, 3,079,285 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 Capital 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.

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; 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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DESCRIPTION OF PREFERRED STOCK

We have the authority to issue up to 5,000,000 shares of preferred stock. As of June 2, 2016, 335,273 shares of our preferred stock were outstanding (see "6% Convertible Exchangeable Preferred Stock" below). The description of preferred stock provisions set forth below is not complete and is subject to and qualified in its entirety by reference to our certificate of incorporation and the certificate of designations relating to each series of preferred stock.

If we offer a specific series of preferred stock under this prospectus, we will describe the terms of the preferred stock in the prospectus supplement for such offering and will file a copy of the certificate establishing the terms of the preferred stock with the SEC. To the extent required, this description will include:

- the title and stated value;
- the number of shares offered, the liquidation preference, if any, per share and the purchase price;
- the dividend rate(s), period(s) and/or payment date(s), or method(s) of calculation for such dividends;
- whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- the procedures for any auction and remarketing, if any;
- the provisions for a sinking fund, if any;
- the provisions for redemption, if applicable;
- any listing of the preferred stock on any securities exchange or market;
- whether the preferred stock will be convertible into our common stock, and, if applicable, the conversion price (or how it will be calculated) and conversion period;
- whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price (or how it will be calculated) and exchange period;
- voting rights, if any, of the preferred stock;
- a discussion of any material and/or special U.S. federal income tax considerations applicable to the preferred stock;
- the relative ranking and preferences of the preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of the affairs of Cyclacel; and

- any material limitations on issuance of any class or series of preferred stock ranking pari passu with or senior to the series of preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of Cyclacel.

We have previously issued 2,990,000 shares of preferred stock in one series, designated as 6% Convertible Exchangeable Preferred Stock, of which 335,273 are currently outstanding.

Transfer Agent

Our transfer agent and registrar for our 6% Convertible Exchangeable Preferred Stock is American Stock Transfer & Trust Company, LLC.

Listing

Our 6% Convertible Exchangeable Preferred Stock is listed for quotation on The NASDAQ Capital Market under the symbol “CYCCP.”

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6% Convertible Exchangeable Preferred Stock

General

Our board of directors has designated 2,990,000 shares of the preferred stock that were issued as convertible preferred stock on November 3, 2004. The shares of convertible preferred stock are duly and validly issued, fully paid and non-assessable. These shares will not have any preemptive rights if we issue other series of preferred stock. The convertible preferred stock is not subject to any sinking fund. We have no obligation to retire the convertible preferred stock. The convertible preferred stock has a perpetual maturity and may remain outstanding indefinitely, subject to the holder's right to convert the convertible preferred stock and our right to cause the conversion of the convertible preferred stock and exchange or redeem the convertible preferred stock at our option. Any convertible preferred stock converted, exchanged or redeemed or acquired by us will, upon cancellation, have the status of authorized but unissued shares of convertible preferred stock. We will be able to reissue these cancelled shares of convertible preferred stock.

Dividends

When and if declared by our board of directors out of the legally available funds, holders of the convertible preferred stock are entitled to receive cash dividends at an annual rate of 6% of the liquidation preference of the convertible preferred stock. Dividends are payable quarterly on the first day of February, May, August and November. If any dividends are not declared, they will accrue and be paid at such later date, if any, as determined by our board of directors. Dividends on the convertible preferred stock will be cumulative from the issue date. Dividends will be payable to holders of record as they appear on our stock books not more than 60 days nor less than 10 days preceding the payment dates, as fixed by our board of directors. If the convertible preferred stock is called for redemption on a redemption date between the dividend record date and the dividend payment date and the holder does not convert the convertible preferred stock (as described below), the holder shall receive the dividend payment together with all other accrued and unpaid dividends on the redemption date instead of receiving the dividend on the dividend date. Dividends payable on the convertible preferred stock for any period greater or less than a full dividend period will be computed on the basis of a 360-day year consisting of twelve 30-day months. Accrued but unpaid dividends will not bear interest.

If we do not pay or set aside cumulative dividends in full on the convertible preferred stock and any other preferred stock ranking on the same basis as to dividends, all dividends declared upon shares of the convertible preferred stock and any other preferred stock ranking on the same basis as to dividends will be declared on a pro rata basis until all accrued dividends are paid in full. For these purposes, "pro rata" means that the amount of dividends declared per share on the convertible preferred stock and any other preferred stock ranking on the same basis as to dividends bear to each other will be the same ratio that accrued and unpaid dividends per share on the shares of the convertible preferred stock and such other preferred stock bear to each other. We will not be able to redeem, purchase or otherwise acquire any of our stock ranking on the same basis as the convertible preferred stock as to dividends or liquidation preferences unless we have paid or set aside full cumulative dividends, if any, accrued on all outstanding shares of convertible preferred stock.

Unless we have paid or set aside cumulative dividends in full on the convertible preferred stock and any other of the convertible preferred stock ranking on the same basis as to dividends:

- we may not declare or pay or set aside dividends on common stock or any other stock ranking junior to the convertible preferred stock as to dividends or liquidation preferences, excluding dividends or distributions of shares, options, warrants or rights to purchase common stock or other stock ranking junior to the convertible preferred stock as to dividends; or

- we will not be able to redeem, purchase or otherwise acquire any of our other stock ranking junior to the convertible preferred stock as to dividends or liquidation preferences, except in very limited circumstances.

Under Delaware law, we may only make dividends or distributions to our stockholders from:

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our surplus; or

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the net profits for the current fiscal year or the fiscal year before which the dividend or distribution is declared under certain circumstances.

As previously disclosed, our Board of Directors did not declare the quarterly cash dividend with respect to each of the four quarters of fiscal year 2009, the first, second and third quarters of fiscal year 2010, the second, third and fourth quarters of fiscal year 2011 and the first, second and third quarters of fiscal year 2012. On December 24, 2015, our Board of Directors did declare a quarterly cash dividend in the amount of $0.15 per share on the Preferred Stock with respect to the fourth quarter of fiscal year 2015. The cash dividend was paid on February 1, 2016 to the holders of record of the Preferred Stock as of the close business on January 21, 2016. In addition, on March 29, 2016, the Board of Directors declared a quarterly dividend payable on May 1, 2016 to the holders of record of the Preferred Stock as of the close of business on April 18, 2016. To the extent that any dividends payable on the Preferred Stock are not paid, such unpaid dividends are accrued. As the Company failed to pay in an aggregate amount equal to at least six quarterly dividends (whether or not consecutive) on the Preferred Stock, the size of the Company's Board was increased by two members and the holders of the Preferred Stock, voting separately as a class, voted on May 24, 2011 and elected two directors to fill the vacancies created thereby, which directorships shall terminate when the Company pays all accrued but unpaid dividends. As of June 2, 2016, approximately $670,000 of dividends remain unpaid.

Conversion

Conversion Rights

Holders of our convertible preferred stock may convert the convertible preferred stock at any time into a number of shares of common stock determined by dividing the $10 liquidation preference by the conversion price of $1,974, being the original conversion price of $2.35 as adjusted following three reverse stock splits, subject to adjustment as described below. This conversion price is equivalent to a conversion rate of approximately 0.00507 shares of common stock for each share of convertible preferred stock. We will not make any adjustment to the conversion price for accrued or unpaid dividends upon conversion. We will not issue fractional shares of common stock upon conversion. However, we will instead pay cash for each fractional share based upon the market price of the common stock on the last business day prior to the conversion date. If we call the convertible preferred stock for redemption, the holder's right to convert the convertible preferred stock will expire at the close of business on the business day immediately preceding the date fixed for redemption, unless we fail to pay the redemption price.

Automatic Conversion

Unless we redeem or exchange the convertible preferred stock, we may elect to convert some or all of the convertible preferred stock into shares of our common stock if the closing price of our common stock has exceeded 150% of the conversion price for at least 20 out of 30 consecutive trading days ending within five trading days prior to the notice of automatic conversion. If we elect to convert less than all of the shares of convertible preferred stock, we shall select the shares to be converted by lot or pro rata or in some other equitable manner in our discretion. On or after November 3, 2007, we may not elect to automatically convert the convertible preferred stock if full cumulative dividends on the convertible preferred stock for all past dividend periods have not been paid or set aside for payment.

Conversion Price Adjustment — General

The conversion price of $1,974 will be adjusted if:

(1)

we divide or distribute common stock on shares of our common stock;

(2)

we subdivide or combine our common stock;

(3)

we issue to all holders of common stock certain rights or warrants to purchase our common stock at less than the current market price;

(4)

we divide or distribute to all holders of our common stock shares of our capital stock or evidences of indebtedness or assets, excluding:

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- those rights, warrants, dividends or distributions referred to in (1) or (3), or

- dividends and distributions paid in cash;

(5) we made a dividend or distribution consisting of cash to all holders of common stock;

(6) we purchase common stock pursuant to a tender offer made by us or any of our subsidiaries; and

(7) a person other than us or any of our subsidiaries makes any payment on a tender offer or exchange offer and, as of the closing of the offer, the board of directors is not recommending rejection of the offer. We will only make this adjustment if the tender or exchange offer increases a person's ownership to more than 25% of our outstanding common stock, and only if the payment per share of common stock exceeds the current market price of our common stock. We will not make this adjustment if the offering documents disclose our plan to engage in any consolidation, merger, or transfer of all or substantially all of our properties and if specified conditions are met.

If we implement a stockholder rights plan, this new rights plan must provide that, upon conversion of the existing convertible preferred stock the holders will receive, in addition to the common stock issuable upon such conversion, the rights under such rights plan regardless of whether the rights have separated from the common stock before the time of conversion. The distribution of rights or warrants pursuant to a stockholder rights plan will not result in an adjustment to the conversion price of the convertible preferred stock until a specified triggering event occurs.

The occurrence and magnitude of certain of the adjustments described above is dependent upon the current market price of our common stock. For these purposes, "current market price" generally means the lesser of:

- the closing sale price on certain specified dates, or

- the average of the closing prices of the common stock for the ten trading day period immediately prior to certain specified dates.

We may make a temporary reduction in the conversion price of the convertible preferred stock if our board of directors determines that this decrease would be in our best interest. We may, at our option, reduce the conversion price if our board of directors deems it advisable to avoid or diminish any income tax to holders of common stock resulting from any dividend or distribution of stock or rights to acquire stock or from any event treated as such for income tax purposes.

Conversion Price Adjustment — Merger, Consolidation or Sale of Assets

If we are involved in a transaction in which shares of our common stock are converted into the right to receive other securities, cash or other property, or a sale or transfer of all or substantially all of our assets under which the holders of our common stock shall be entitled to receive other securities, cash or other property, then appropriate provision shall be made so that the shares of convertible preferred stock will convert into:

(1) if the transaction is a common stock fundamental change, as defined below, common stock of the kind received by holders of common stock as a result of common stock fundamental change in accordance with paragraph (1) below under the subsection entitled "— Fundamental Change Conversion Price Adjustments," and

(2)

if the transaction is not a common stock fundamental change, and subject to funds being legally available at conversion, the kind and amount of the securities, cash or other property that would have been receivable upon the recapitalization, reclassification, consolidation, merger, sale, transfer or share exchange by a holder of the number of shares of common stock issuable upon conversion of the convertible preferred stock immediately prior to the recapitalization, reclassification, consolidation, merger, sale, transfer or share exchange, after giving effect to any adjustment in the conversion price in accordance with paragraph (2) below under the subsection entitled "— Fundamental Change Conversion Price Adjustments."

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The company formed by the consolidation, merger, asset acquisition or share acquisition shall provide for this right in its organizational document. This organizational document shall also provide for adjustments so that the organizational document shall be as nearly practicably equivalent to adjustments in this section for events occurring after the effective date of the organizational document.

The following types of transactions, among others, would be covered by this adjustment:

(1)
we recapitalize or reclassify our common stock, except for

- a change in par value,
- a change from par value to no par value,
- a change from no par value to par value, or
- a subdivision or combination of our common stock.

(2)
we consolidate or merge into any other person, or any merger of another person into us, except for a merger that does not result in a reclassification, conversion, exchange or cancellation of common stock,

(3)
we sell, transfer or lease all or substantially all of our assets and holders of our common stock become entitled to receive other securities, cash or other property, or

(4)
undertake any compulsory share exchange.

Fundamental Change Conversion Price Adjustments

If a fundamental change occurs, the conversion price will be adjusted as follows:

(1)
in the case of a common stock fundamental change, the conversion price shall be the conversion price after giving effect to any other prior adjustments effected pursuant to the preceding paragraphs, multiplied by a fraction, the numerator of which is the purchaser stock price, as defined below, and the denominator of which is the applicable price, as defined below. However, in the event of a common stock fundamental change in which:

- 100% of the value of the consideration received by a holder of our common stock is common stock of the successor, acquirer or other third party, and cash, if any, paid with respect to any fractional interests in such common stock resulting from such common stock fundamental change,
- all of our common stock shall have been exchanged for, converted into or acquired for, common stock of the successor, acquirer or other third party, and any cash with respect to fractional interests, and
-

the conversion price shall be the conversion price in effect immediately prior to such common stock fundamental change multiplied by a fraction, the numerator of which is one (1) and the denominator of which is the number of shares of common stock of the successor, acquirer or other third party received by a holder of one share of our common stock as a result of the common stock fundamental change;

(2)
in the case of a non-stock fundamental change, the conversion price shall be the lower of:

•
the conversion price after giving effect to any other prior adjustments effected pursuant to the preceding paragraph and

•
the product of

A.
the applicable price, and

B.
a fraction, the numerator of which is $10 and the denominator of which is (x) the amount of the redemption price for one share of convertible preferred stock if the redemption date were the date of the non-stock fundamental change (or if the date of such non-stock fundamental change falls within the period beginning on the first issue date of the convertible preferred stock through October 31, 2005, the twelve-month

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period commencing November 1, 2005 and the twelve-month period commencing November 1, 2006, the product of 106.0%, 105.4% or 104.8%, respectively, and $10) plus (y) any then-accrued and unpaid distributions on one share of convertible preferred stock.

Holders of convertible preferred stock may receive significantly different consideration upon conversion depending upon whether a fundamental change is a non-stock fundamental change or a common stock fundamental change. In the event of a non-stock fundamental change, the shares of convertible preferred stock will convert into stock and other securities or property or assets, including cash, determined by the number of shares of common stock receivable upon conversion at the conversion price as adjusted in accordance with (2) above. In the event of a common stock fundamental change, under certain circumstances, the holder of convertible preferred stock will receive different consideration depending on whether the holder converts his or her shares of convertible preferred stock on or after the common stock fundamental change.

Definitions for the Fundamental Change Adjustment Provision

“applicable price” means:

- in a non-stock fundamental change in which the holders of common stock receive only cash, the amount of cash received by a holder of one share of common stock, and

- in the event of any other fundamental change, the average of the daily closing price for one share of common stock during the 10 trading days immediately prior to the record date for the determination of the holders of common stock entitled to receive cash, securities, property or other assets in connection with the fundamental change or, if there is no such record date, prior to the date upon which the holders of common stock shall have the right to receive such cash, securities, property or other assets.

“common stock fundamental change” means any fundamental change in which more than 50% of the value, as determined in good faith by our board of directors, of the consideration received by holders of our common stock consists of common stock that, for the 10 trading days immediately prior to such fundamental change, has been admitted for listing or admitted for listing subject to notice of issuance on a national securities exchange or quoted on The NASDAQ National Market, except that a fundamental change shall not be a common stock fundamental change unless either:

- we continue to exist after the occurrence of the fundamental change and the outstanding convertible preferred stock continues to exist as outstanding convertible preferred stock, or

- not later than the occurrence of the fundamental change, the outstanding convertible preferred stock is converted into or exchanged for shares of preferred stock, which preferred stock has rights, preferences and limitations substantially similar, but no less favorable, to those of the convertible preferred stock.

“fundamental change” means the occurrence of any transaction or event or series of transactions or events pursuant to which all or substantially all of our common stock shall be exchanged for, converted into, acquired for or shall constitute solely the right to receive cash, securities, property or other assets, whether by means of an exchange offer, liquidation, tender offer, consolidation, merger, combination, reclassification, recapitalization or otherwise. However, for purposes of adjustment of the conversion price, in the case of any series of transactions or events, the fundamental change shall be deemed to have occurred when substantially all of the common stock shall have been exchanged for, converted into or acquired for, or shall constitute solely the right to receive, such cash, securities, property or other assets, but the adjustment shall be based upon the consideration that the holders of our common stock received in the transaction or event as a result of which more than 50% of our common stock shall have been exchanged for, converted into or acquired for, or shall constitute solely the right to receive, such cash, securities, property or other assets.

“non-stock fundamental change” means any fundamental change other than a common stock fundamental change.

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"purchaser stock price" means the average of the daily closing price for one share of the common stock received by holders of the common stock in the common stock fundamental change during the 10 trading days immediately prior to the date fixed for the determination of the holders of the common stock entitled to receive such common stock or, if there is no such date, prior to the date upon which the holders of the common stock shall have the right to receive such common stock.

Liquidation Rights

In the event of our voluntary or involuntary dissolution, liquidation, or winding up, the holders of the convertible preferred stock shall receive a liquidation preference of $10 per share and all accrued and unpaid dividends through the distribution date. Holders of any class or series of preferred stock ranking on the same basis as your convertible preferred stock as to liquidation shall also be entitled to receive the full respective liquidation preferences and any accrued and unpaid dividends through the distribution date. Only after the preferred stock holders have received their liquidation preference and any accrued and unpaid dividends will we distribute assets to common stock holders or any of our other stock ranking junior to the shares of convertible preferred stock upon liquidation. If upon such dissolution, liquidation or winding up, we do not have enough assets to pay in full the amounts due on the convertible preferred stock and any other preferred stock ranking on the same basis with the convertible preferred stock as to liquidation, the holders of the convertible preferred stock and such other preferred stock will share ratably in any such distributions of our assets:

- first in proportion to the liquidation preferences until the preferences are paid in full, and

- then in proportion to the amounts of accrued but unpaid dividends.

After we pay any liquidation preference and accrued dividends, holders of the convertible preferred stock will not be entitled to participate any further in the distribution of our assets. The following events will not be deemed to be a dissolution, liquidation or winding up of Cyclacel:

- the sale of all or substantially all of the assets;

- our merger or consolidation into or with any other corporation; or

- our liquidation, dissolution, winding up or reorganization immediately followed by a reincorporation as another corporation.

Optional Redemption

We may redeem the convertible preferred stock, out of legally available funds, in whole or in part, at our option, at the redemption prices listed below. The redemption price for the 12-month period beginning: November 1, 2012 is $10.12; November 1, 2013 is $10.06; and $10.00 at November 1, 2014 and thereafter. In each case we will pay accrued and unpaid dividends to, but excluding, the redemption date. We are required to give notice of redemption not more than 60 and not less than 20 days before the redemption date.

If we redeem less than all of the shares of convertible preferred stock, we shall select the shares to be redeemed by lot or pro rata or in some other equitable manner in our sole discretion.

Exchange Provisions

We may exchange the convertible preferred stock in whole, but not in part, for debentures on any dividend payment date on or after November 1, 2005 at the rate of $10 principal amount of debentures for each outstanding share of convertible preferred stock. Debentures will be issuable in denominations of $1,000 and integral multiples of $1,000, as discussed in the section entitled "Description of Debentures" below. If the exchange results in an amount of debentures that is not an integral multiple of $1,000, we will pay in cash an amount in excess of the closest integral

multiple of $1,000. We will mail written notice of our intention to exchange the convertible preferred stock to each record holder not less than 30 nor more than 60 days prior to the exchange date.

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We refer to the date fixed for exchange of the convertible preferred stock for debentures as the "exchange date." On the exchange date, the holder's rights as a stockholder of Cyclacel shall cease, the shares of convertible preferred stock will no longer be outstanding, and will only represent the right to receive the debentures and any accrued and unpaid dividends, without interest. We may not exercise our option to exchange the convertible preferred stock for the debentures if:

- full cumulative dividends on the convertible preferred stock to the exchange date have not been paid or set aside for payment, or

- an event of default under the indenture would occur on conversion, or has occurred and is continuing.

Voting Rights

Holders of our convertible preferred stock have no voting rights except as described below or as required by law. Shares of our convertible preferred stock held by us or any entity controlled by us will not have any voting rights.

If we have not paid dividends on the convertible preferred stock or on any outstanding shares of preferred stock ranking on the same basis as to dividends with the convertible preferred stock in an aggregate amount equal to at least six quarterly dividends whether or not consecutive, we will increase the size of our board of directors by two additional directors. So long as dividends remain due and unpaid, holders of the convertible preferred stock, voting separately as a class with holders of preferred stock ranking on the same basis as to dividends having like voting rights, will be entitled to elect two additional directors at any meeting of stockholders at which directors are to be elected. These directors will be appointed to classes on the board as determined by our board of directors. These voting rights will terminate when we have declared and either paid or set aside for payment all accrued and unpaid dividends. The terms of office of all directors so elected will terminate immediately upon the termination of these voting rights.

We have not declared dividends with respect to at least six quarters and, therefore, the holders of the preferred stock, voting separately as a class, are entitled to elect, and have elected, two directors.

Without the vote or consent of the holders of at least a majority of the shares of convertible preferred stock, we may not:

- adversely change the rights, preferences and limitations of the convertible preferred stock by modifying our certificate of incorporation or bylaws, or

- authorize, issue, reclassify any of our authorized stock into, increase the authorized amount of, or authorize or issue any convertible obligation or security or right to purchase, any class of stock that ranks senior to the convertible preferred stock as to dividends or distributions of assets upon liquidation, dissolution or winding up of the stock.

No class vote on the part of convertible preferred stock shall be required (except as otherwise required by law or resolution of our board of directors) in connection with the authorization, issuance or increase in the authorized amount of any shares of capital stock ranking junior to or on parity with the convertible preferred stock both as to the payment of dividends and as to distribution of assets upon our liquidation, dissolution or winding up, whether voluntary or involuntary, including our common stock and the convertible preferred stock.

In addition, without the vote or consent of the holders of at least a majority of the shares of convertible preferred stock we may not:

- enter into a share exchange that affects the convertible preferred stock,

- consolidate with or merge into another entity, or

- permit another entity to consolidate with or merge into us,

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unless the convertible preferred stock remains outstanding and its rights, privileges and preferences are unaffected or it is converted into or exchanged for convertible preferred stock of the surviving entity having rights, preferences and limitations substantially similar, but no less favorable, to the convertible preferred stock.

In determining a majority under these voting provisions, holders of convertible preferred stock will vote together with holders of any other preferred stock that rank on parity as to dividends and that have like voting rights.

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DESCRIPTION OF WARRANTS

General

We may issue warrants to purchase shares of our common stock, preferred stock and/or debt securities in one or more series together with other securities or separately, as described in the applicable prospectus supplement. Below is a description of certain general terms and provisions of the warrants that we may offer. Particular terms of the warrants will be described in the warrant agreements and the prospectus supplement relating to the warrants.

The applicable prospectus supplement will contain, where applicable, the following terms of and other information relating to the warrants:

- the specific designation and aggregate number of, and the price at which we will issue, the warrants;
- the currency or currency units in which the offering price, if any, and the exercise price are payable;
- the designation, amount and terms of the securities purchasable upon exercise of the warrants;
- if applicable, the exercise price for shares of our common stock and the number of shares of common stock to be received upon exercise of the warrants;
- if applicable, the exercise price for shares of our preferred stock, the number of shares of preferred stock to be received upon exercise, and a description of that series of our preferred stock;
- if applicable, the exercise price for our debt securities, the amount of debt securities to be received upon exercise, and a description of that series of debt securities;
- the date on which the right to exercise the warrants will begin and the date on which that right will expire or, if you may not continuously exercise the warrants throughout that period, the specific date or dates on which you may exercise the warrants;
- whether the warrants will be issued in fully registered form or bearer form, in definitive or global form or in any combination of these forms, although, in any case, the form of a warrant included in a unit will correspond to the form of the unit and of any security included in that unit;
- any applicable material U.S. federal income tax consequences;
- the identity of the warrant agent for the warrants and of any other depositaries, execution or paying agents, transfer agents, registrars or other agents;
- the proposed listing, if any, of the warrants or any securities purchasable upon exercise of the warrants on any securities exchange;

- if applicable, the date from and after which the warrants and the common stock, preferred stock and/or debt securities will be separately transferable;

- if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;

- information with respect to book-entry procedures, if any;

- the anti-dilution provisions of the warrants, if any;

- any redemption or call provisions;

- whether the warrants may be sold separately or with other securities as parts of units; and

- any additional terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants. We will describe the particular terms of any warrants that we may offer under this prospectus in more detail in the applicable prospectus supplement and the related warrant agreements and warrant certificates.

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Outstanding Warrants

The following is a brief summary of the terms of our outstanding warrants.

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July 2011 Warrants — On July 7, 2011, as part of an underwritten offering for an aggregate of 90,686 units, we sold warrants to purchase up to an aggregate of 45,343 shares of common stock, each warrant to purchase 0.5 shares of common stock at an exercise price of $114.24 per share, such warrants expiring at 5:00 p.m. Eastern Time on July 7, 2016. We refer to these warrants as the July 2011 Warrants. As of June 2, 2016, there were 45,343 shares available for purchase under the October 2010 Warrants.

Exercisability. The exercise price and number of shares of common stock issuable upon exercise of all of the warrants may be adjusted in certain circumstances, including in the event of a stock dividend, or our recapitalization, reorganization, merger or consolidation.

Exercise of Warrants. All of the warrants may be exercised upon surrender of the warrant on or prior to the expiration date at the offices of the warrant agent, with the exercise form set forth in the warrant completed and executed as indicated, either accompanied by full payment of the exercise price, by certified check payable to us, for the number of warrants being exercised or, under certain circumstances, by means of a cashless exercise, as provided for in the warrant. Notwithstanding the foregoing, the holder will not be required to physically surrender the warrant unless and until the aggregate warrant shares represented by the warrant are exercised. The warrants are exercisable by delivery of a written notice, with payment made within two trading days of the delivery of the notice of exercise.

Cashless Exercise. If, at any time during the exercisability period of any of the warrants, the holder is not permitted to sell shares of common stock issuable upon exercise of the relevant warrant pursuant to the registration statement or an exemption from registration is not available, and the fair market value of our common stock exceeds the exercise price of the warrants, the holder may elect to effect a cashless exercise of the warrants, in whole or in part, by surrendering the warrants to us, together with delivery to us of a duly executed exercise notice, and canceling a portion of the relevant warrant in payment of the purchase price payable in respect of the number of shares of our common stock purchased upon such exercise.

Buy-in Right. If we fail to issue shares of common stock to the holder of a warrant within three business days of our receipt of a duly executed exercise notice, then the holder or any third party on behalf of the holder may, for such holder's account, purchase in an open market transaction or otherwise, shares of common stock to deliver in satisfaction of a sale by the holder of shares of common stock issuable upon such exercise that the holder anticipated receiving from us. At such holder's request and in its discretion, either (i) pay cash to the holder in an amount equal to the holder's total purchase price (including brokerage commissions, if any) for the shares of common stock so purchased (the "Buy-In Price"), at which point the Company's obligation to deliver such certificate (and to issue such shares of common stock) shall terminate, or (ii) promptly honor its obligation to deliver to the holder a certificate or certificates representing such shares and pay cash to the holder in an amount equal to the excess (if any) of the Buy-In Price over the product of (A) such number of shares of common stock, times (B) the Closing Bid Price (as defined in such warrants) on the date of exercise.

Transferability. Subject to applicable laws and the restriction on transfer set forth in the relevant subscription agreement, none of the warrants may be transferred by the holder without our consent, such consent not to be unreasonably withheld or delayed, upon surrender of the warrants to us together with the appropriate instruments of transfer.

Exchange Listing. We do not plan on making an application to list any of the warrants on The NASDAQ Capital Market, any national securities exchange or other nationally recognized trading system. The common stock underlying the warrants is listed on the NASDAQ Capital Market.

Fundamental Transactions. In the event of any fundamental transaction, as described in the warrants, and generally including any merger with or into another entity (whether or not we are the surviving entity but excluding a migratory merger effected solely for the purpose of changing our jurisdiction of incorporation), sale of all or substantially all of our assets, tender offer or exchange offer, our consummation of a stock purchase agreement or other business combination (including, without limitation, a reorganization, recapitalization, spin-off or scheme of arrangement) or reclassification of our common

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stock, then upon any subsequent exercise of a warrant, the holder shall have the right to receive, as alternative consideration, for each share of our common stock that would have been issuable upon such exercise immediately prior to the occurrence of such fundamental transaction, the number of shares of common stock of the successor or acquiring corporation or of Cyclacel, if it is the surviving corporation, and any additional consideration receivable upon or as a result of such transaction by a holder of the number of shares of our common stock for which the warrant is exercisable immediately prior to such event. Notwithstanding the foregoing, the holders of the warrants and the Option Warrants, in the event of a fundamental transaction (i) in which holders of common stock receive all cash or substantially all cash or (ii) with a person whose common stock or equivalent equity security is not quoted or listed on an eligible market, as defined in such warrant, and, in either case, at the request of the holder delivered within 30 days after consummation of the fundamental transaction, we (or our successor entity) must purchase such warrant from the holder by paying to the holder, within seven business days after such request (or, if later, on the effective date of the fundamental transaction), cash in an amount equal to the Black Scholes value, as defined in such warrant, of the remaining unexercised portion of such warrant or Option Warrant on the date of such fundamental transaction. Fundamental transactions shall not include any transaction in which the Company is not a voluntary party thereto.

Waivers and Amendments. The provisions of each warrant may be amended and we may not take any action prohibited by such warrant, or omit to perform any act required to be performed pursuant to such warrant, only with the written consent of the holder of that warrant.

Rights as a Stockholder. The warrant holders do not have the rights or privileges of holders of common stock, including any voting rights, until they exercise their warrants and receive shares of common stock. After the issuance of shares of common stock upon exercise of the warrants, each holder will be entitled to one vote for each share held of record on all matters to be voted on by stockholders.

No Fractional Shares. No fractional shares will be issued upon exercise of any of the warrants. We will pay to the holder thereof, in lieu of the issuance of any fractional share which is otherwise issuable to the warrant holder, an amount in cash based on the market value of the common stock on the last trading day prior to the exercise date.

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DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information we include in any applicable prospectus supplements, summarizes the material terms and provisions of the debt securities that we may offer under this prospectus. While the terms we have summarized below will apply generally to any future debt securities we may offer pursuant to this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement. If we so indicate in a prospectus supplement, the terms of any debt securities offered under such prospectus supplement may differ from the terms we describe below, and to the extent the terms set forth in a prospectus supplement differ from the terms described below, the terms set forth in the prospectus supplement shall control.

We may sell from time to time, in one or more offerings under this prospectus, debt securities, which may be senior or subordinated. We will issue any such senior debt securities under a senior indenture that we will enter into with a trustee to be named in the senior indenture. We will issue any such subordinated debt securities under a subordinated indenture, which we will enter into with a trustee to be named in the subordinated indenture. We have filed forms of these documents as exhibits to the registration statement, of which this prospectus is a part. We use the term "indentures" to refer to either the senior indenture or the subordinated indenture, as applicable. The indentures will be qualified under the Trust Indenture Act of 1939, as in effect on the date of the indenture. We use the term "debenture trustee" to refer to either the trustee under the senior indenture or the trustee under the subordinated indenture, as applicable.

The following summaries of material provisions of the senior debt securities, the subordinated debt securities and the indentures are subject to, and qualified in their entirety by reference to, all the provisions of the indenture applicable to a particular series of debt securities.

General

Each indenture provides that debt securities may be issued from time to time in one or more series and may be denominated and payable in foreign currencies or units based on or relating to foreign currencies. Neither indenture limits the amount of debt securities that may be issued thereunder, and each indenture provides that the specific terms of any series of debt securities shall be set forth in, or determined pursuant to, an authorizing resolution and/or a supplemental indenture, if any, relating to such series.

We will describe in each prospectus supplement the following terms relating to a series of debt securities:

- the title or designation;
- the aggregate principal amount and any limit on the amount that may be issued;
- the currency or units based on or relating to currencies in which debt securities of such series are denominated and the currency or units in which principal or interest or both will or may be payable;
- whether we will issue the series of debt securities in global form, the terms of any global securities and who the depositary will be;
- the maturity date and the date or dates on which principal will be payable;
- the interest rate, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the date or dates interest will be payable and the record dates for interest payment dates or the method for determining such dates;

- whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;

- the terms of the subordination of any series of subordinated debt;

- the place or places where payments will be payable;

- our right, if any, to defer payment of interest and the maximum length of any such deferral period;

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- the date, if any, after which, and the price at which, we may, at our option, redeem the series of debt securities pursuant to any optional redemption provisions;

- the date, if any, on which, and the price at which we are obligated, pursuant to any mandatory sinking fund provisions or otherwise, to redeem, or at the holder's option to purchase, the series of debt securities;

- whether the indenture will restrict our ability to pay dividends, or will require us to maintain any asset ratios or reserves;

- whether we will be restricted from incurring any additional indebtedness;

- a discussion on any material or special U.S. federal income tax considerations applicable to a series of debt securities;

- the denominations in which we will issue the series of debt securities, if other than denominations of $1,000 and any integral multiple thereof; and

- any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities.

We may issue debt securities that provide for an amount less than their stated principal amount to be due and payable upon declaration of acceleration of their maturity pursuant to the terms of the indenture. We will provide you with information on the federal income tax considerations and other special considerations applicable to any of these debt securities in the applicable prospectus supplement.

Conversion or Exchange Rights

We will set forth in the prospectus supplement the terms, if any, on which a series of debt securities may be convertible into or exchangeable for our common stock or our other securities. We will include provisions as to whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock or our other securities that the holders of the series of debt securities receive would be subject to adjustment.

Consolidation, Merger or Sale; No Protection in Event of a Change of Control or Highly Leveraged Transaction

The indentures do not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of all or substantially all of our assets. However, any successor to or acquirer of such assets must assume all of our obligations under the indentures or the debt securities, as appropriate.

Unless we state otherwise in the applicable prospectus supplement, the debt securities will not contain any provisions that may afford holders of the debt securities protection in the event we have a change of control or in the event of a highly leveraged transaction (whether or not such transaction results in a change of control), which could adversely affect holders of debt securities.

Events of Default Under the Indenture

The following are events of default under the indentures with respect to any series of debt securities that we may issue:

- if we fail to pay interest when due and our failure continues for 90 days and the time for payment has not been extended or deferred;

- if we fail to pay the principal, or premium, if any, when due and the time for payment has not been extended or delayed;

- if we fail to observe or perform any other covenant set forth in the debt securities of such series or the applicable indentures, other than a covenant specifically relating to and for the benefit of holders of another series of debt securities, and our failure continues for 90 days after we receive written notice from the debenture trustee or holders of not less than a majority in aggregate principal amount of the outstanding debt securities of the applicable series; and

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- if specified events of bankruptcy, insolvency or reorganization occur as to us.

No event of default with respect to a particular series of debt securities (except as to certain events of bankruptcy, insolvency or reorganization) necessarily constitutes an event of default with respect to any other series of debt securities. The occurrence of an event of default may constitute an event of default under any bank credit agreements we may have in existence from time to time. In addition, the occurrence of certain events of default or an acceleration under the indenture may constitute an event of default under certain of our other indebtedness outstanding from time to time.

If an event of default with respect to debt securities of any series at the time outstanding occurs and is continuing, then the trustee or the holders of not less than a majority in principal amount of the outstanding debt securities of that series may, by a notice in writing to us (and to the debenture trustee if given by the holders), declare to be due and payable immediately the principal (or, if the debt securities of that series are discount securities, that portion of the principal amount as may be specified in the terms of that series) of and premium and accrued and unpaid interest, if any, on all debt securities of that series.

Before a judgment or decree for payment of the money due has been obtained with respect to debt securities of any series, the holders of a majority in principal amount of the outstanding debt securities of that series (or, at a meeting of holders of such series at which a quorum is present, the holders of a majority in principal amount of the debt securities of such series represented at such meeting) may rescind and annul the acceleration if all events of default, other than the non-payment of accelerated principal, premium, if any, and interest, if any, with respect to debt securities of that series, have been cured or waived as provided in the applicable indenture (including payments or deposits in respect of principal, premium or interest that had become due other than as a result of such acceleration). We refer you to the prospectus supplement relating to any series of debt securities that are discount securities for the particular provisions relating to acceleration of a portion of the principal amount of such discount securities upon the occurrence of an event of default.

Subject to the terms of the indentures, if an event of default under an indenture shall occur and be continuing, the debenture trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the debenture trustee reasonable indemnity. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the debenture trustee, or exercising any trust or power conferred on the debenture trustee, with respect to the debt securities of that series, provided that:

- the direction so given by the holder is not in conflict with any law or the applicable indenture; and

- subject to its duties under the Trust Indenture Act, the debenture trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

A holder of the debt securities of any series will only have the right to institute a proceeding under the indentures or to appoint a receiver or trustee, or to seek other remedies if:

- the holder previously has given written notice to the debenture trustee of a continuing event of default with respect to that series;

- the holders of at least a majority in aggregate principal amount of the outstanding debt securities of that series have made written request, and such holders have offered reasonable indemnity to the debenture trustee to institute the proceeding as trustee; and

- the debenture trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series (or at a meeting of holders of such series at which a quorum is present, the holders of a majority in principal amount of the debt securities of such series represented at such meeting) other conflicting directions within 60 days after the notice, request and offer.

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These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities.

We will periodically file statements with the applicable debenture trustee regarding our compliance with specified covenants in the applicable indenture.

Modification of Indenture; Waiver

The debenture trustee and we may change the applicable indenture without the consent of any holders with respect to specific matters, including:

- to fix any ambiguity, defect or inconsistency in the indenture; and

- to change anything that does not materially adversely affect the interests of any holder of debt securities of any series issued pursuant to such indenture.

In addition, under the indentures, the rights of holders of a series of debt securities may be changed by us and the debenture trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series (or, at a meeting of holders of such series at which a quorum is present, the holders of a majority in principal amount of the debt securities of such series represented at such meeting) that is affected. However, the debenture trustee and we may make the following changes only with the consent of each holder of any outstanding debt securities affected:

- extending the fixed maturity of the series of debt securities;

- reducing the principal amount, reducing the rate of or extending the time of payment of interest, or any premium payable upon the redemption of any debt securities;

- reducing the principal amount of discount securities payable upon acceleration of maturity;

- making the principal of or premium or interest on any debt security payable in currency other than that stated in the debt security; or

- reducing the percentage of debt securities, the holders of which are required to consent to any amendment or waiver.

Except for certain specified provisions, the holders of at least a majority in principal amount of the outstanding debt securities of any series (or, at a meeting of holders of such series at which a quorum is present, the holders of a majority in principal amount of the debt securities of such series represented at such meeting) may on behalf of the holders of all debt securities of that series waive our compliance with provisions of the indenture. The holders of a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all the debt securities of such series waive any past default under the indenture with respect to that series and its consequences, except a default in the payment of the principal of, premium or any interest on any debt security of that series or in respect of a covenant or provision, which cannot be modified or amended without the consent of the holder of each outstanding debt security of the series affected; provided, however, that the holders of a majority in principal amount of the outstanding debt securities of any series may rescind an acceleration and its consequences, including any related payment default that resulted from the acceleration.

Discharge

Each indenture provides that we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for obligations to:

- register the transfer or exchange of debt securities of the series;
- replace stolen, lost or mutilated debt securities of the series;
- maintain paying agencies;
- hold monies for payment in trust;
- compensate and indemnify the trustee; and

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- appoint any successor trustee.

In order to exercise our rights to be discharged with respect to a series, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, the premium, if any, and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we otherwise specify in the applicable prospectus supplement, in denominations of $1,000 and any integral multiple thereof. The indentures provide that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company or another depositary named by us and identified in a prospectus supplement with respect to that series.

At the option of the holder, subject to the terms of the indentures and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indentures and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange or in the applicable indenture, we will make no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

If we elect to redeem the debt securities of any series, we will not be required to:

- issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or

- register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Debenture Trustee

The debenture trustee, other than during the occurrence and continuance of an event of default under the applicable indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the debenture trustee under such indenture must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs. Subject to this provision, the debenture trustee is under no obligation to exercise any of the powers given it by the indentures at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

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We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, will we make interest payments by check which we will mail to the holder. Unless we otherwise indicate in a prospectus supplement, we will designate the corporate trust office of the debenture trustee in the City of New York as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the debenture trustee for the payment of the principal of or any premium or interest on any debt securities which remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the security thereafter may look only to us for payment thereof.

Governing Law

The indentures and the debt securities will be governed by and construed in accordance with the laws of the State of New York, except to the extent that the Trust Indenture Act is applicable.

Subordination of Subordinated Debt Securities

Our obligations pursuant to any subordinated debt securities will be unsecured and will be subordinate and junior in priority of payment to certain of our other indebtedness to the extent described in a prospectus supplement. The subordinated indenture does not limit the amount of senior indebtedness we may incur. It also does not limit us from issuing any other secured or unsecured debt.

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DESCRIPTION OF RIGHTS

General

We may issue rights to our stockholders to purchase shares of our common stock, preferred stock or the other securities described in this prospectus. We may offer rights separately or together with one or more additional rights, debt securities, preferred stock, common stock, warrants or purchase contracts, or any combination of those securities in the form of units, as described in the applicable prospectus supplement. Each series of rights will be issued under a separate rights agreement to be entered into between us and a bank or trust company, as rights agent. The rights agent will act solely as our agent in connection with the certificates relating to the rights of the series of certificates and will not assume any obligation or relationship of agency or trust for or with any holders of rights certificates or beneficial owners of rights. The following description sets forth certain general terms and provisions of the rights to which any prospectus supplement may relate. The particular terms of the rights to which any prospectus supplement may relate and the extent, if any, to which the general provisions may apply to the rights so offered will be described in the applicable prospectus supplement. To the extent that any particular terms of the rights, rights agreement or rights certificates described in a prospectus supplement differ from any of the terms described below, then the terms described below will be deemed to have been superseded by that prospectus supplement. We encourage you to read the applicable rights agreement and rights certificate for additional information before you decide whether to purchase any of our rights.

We will provide in a prospectus supplement the following terms of the rights being issued:

- the date of determining the stockholders entitled to the rights distribution;
- the aggregate number of shares of common stock, preferred stock or other securities purchasable upon exercise of the rights;
- the exercise price;
- the aggregate number of rights issued;
- whether the rights are transferrable and the date, if any, on and after which the rights may be separately transferred;
- the date on which the right to exercise the rights will commence, and the date on which the right to exercise the rights will expire;
- the method by which holders of rights will be entitled to exercise;
- the conditions to the completion of the offering, if any;
- the withdrawal, termination and cancellation rights, if any;
- whether there are any backstop or standby purchaser or purchasers and the terms of their commitment, if any;

- whether stockholders are entitled to oversubscription rights, if any;

- any applicable U.S. federal income tax considerations; and

- any other terms of the rights, including terms, procedures and limitations relating to the distribution, exchange and exercise of the rights, as applicable.

Each right will entitle the holder of rights to purchase for cash the principal amount of shares of common stock, preferred stock or other securities at the exercise price provided in the applicable prospectus supplement. Rights may be exercised at any time up to the close of business on the expiration date for the rights provided in the applicable prospectus supplement.

Holders may exercise rights as described in the applicable prospectus supplement. Upon receipt of payment and the rights certificate properly completed and duly executed at the corporate trust office of the rights agent or any other office indicated in the prospectus supplement, we will, as soon as practicable, forward the shares of common stock, preferred stock or other securities, as applicable, purchasable upon

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exercise of the rights. If less than all of the rights issued in any rights offering are exercised, we may offer any unsubscribed securities directly to persons other than stockholders, to or through agents, underwriters or dealers or through a combination of such methods, including pursuant to standby arrangements, as described in the applicable prospectus supplement.

Rights Agent

The rights agent for any rights we offer will be set forth in the applicable prospectus supplement.

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DESCRIPTION OF PURCHASE CONTRACTS

General

We may issue purchase contracts, including contracts obligating holders to purchase from us, and for us to sell to holders, a specific or variable number of our debt securities, shares of common stock, preferred stock, warrants or rights, or securities of an entity unaffiliated with us, or any combination of the above, at a future date or dates. Alternatively, the purchase contracts may obligate us to purchase from holders, and obligate holders to sell to us, a specific or variable number of our debt securities, shares of common stock, preferred stock, warrants, rights or other property, or any combination of the above. The price of the securities or other property subject to the purchase contracts may be fixed at the time the purchase contracts are issued or may be determined by reference to a specific formula described in the purchase contracts. We may issue purchase contracts separately or as a part of units each consisting of a purchase contract and one or more of our other securities described in this prospectus or securities of third parties, including U.S. Treasury securities, securing the holder's obligations under the purchase contract. The purchase contracts may require us to make periodic payments to holders or vice versa and the payments may be unsecured or pre-funded on some basis. The purchase contracts may require holders to secure the holder's obligations in a manner specified in the applicable prospectus supplement.

The applicable prospectus supplement will describe the terms of any purchase contracts in respect of which this prospectus is being delivered, including, to the extent applicable, the following:

- whether the purchase contracts obligate the holder or us to purchase or sell, or both purchase and sell, the securities subject to purchase under the purchase contract, and the nature and amount of each of those securities, or the method of determining those amounts;

- whether the purchase contracts are to be prepaid;

- whether the purchase contracts are to be settled by delivery, or by reference or linkage to the value, performance or level of the securities subject to purchase under the purchase contract;

- any acceleration, cancellation, termination or other provisions relating to the settlement of the purchase contracts;

- any applicable U.S. federal income tax considerations; and

- whether the purchase contracts will be issued in fully registered or global form.

The preceding description sets forth certain general terms and provisions of the purchase contracts to which any prospectus supplement may relate. The particular terms of the purchase contracts to which any prospectus supplement may relate and the extent, if any, to which the general provisions may apply to the purchase contracts so offered will be described in the applicable prospectus supplement. To the extent that any particular terms of the purchase contracts described in a prospectus supplement differ from any of the terms described above, then the terms described above will be deemed to have been superseded by that prospectus supplement. We encourage you to read the applicable purchase contract for additional information before you decide whether to purchase any of our purchase contracts.

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DESCRIPTION OF UNITS

We may issue units consisting of common stock, preferred stock, warrants, rights, purchase contracts and/or debt securities for the purchase of common stock, preferred stock, warrants, rights, purchase contracts and/or debt securities in one or more series. In this prospectus, we have summarized certain general features of the units.

We will evidence each series of units by unit certificates that we will issue under a separate agreement. We will enter into the unit agreements with a unit agent. Each unit agent will be a bank or trust company that we select. We will indicate the name and address of the unit agent in the applicable prospectus supplement relating to a particular series of units.

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LEGAL MATTERS

Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., New York, New York, will provide us with an opinion as to the legal matters in connection with the securities we are offering.

EXPERTS

The consolidated financial statements of Cyclacel Pharmaceuticals, Inc., appearing in our Annual Report on Form 10-K for the fiscal years ended December 31, 2015 and 2014, have been audited by RSM US LLP, independent registered public accounting firm, as set forth in their report thereon, 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.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports and other information with the SEC. These filings contain important information that does not appear in this prospectus. For further information about us, you may read and copy any reports, statements and other information filed by us at the SEC's Public Reference Room at 100 F Street, N.E., Room 1580, Washington, D.C. 20549-0102. You may obtain further information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. Our SEC filings are also available on the SEC Internet site at http://www.sec.gov, which contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC.

INCORPORATION OF DOCUMENTS BY REFERENCE

The SEC allows us to "incorporate by reference" the information we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus and information we file later with the SEC will automatically update and supersede this information. The documents we are incorporating by reference as of their respective dates of filing are:

- Our Annual Report on Form 10-K for the year ended December 31, 2015, filed on March 29, 2016;

- Our Quarterly Report on Form10-Q for the quarter ended March 31, 2016, filed on May 13, 2016;

- Our Current Reports on Form 8-K filed on February 5, 2016, March 24, 2016, April 11, 2016, May 11, 2016, and May 27, 2016 (except for the information furnished under Items 2.02 or 7.01 and the exhibits furnished thereto);

- Our definitive Proxy Statement relating to our 2016 annual meeting of stockholders filed on April 11, 2016;

- 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.

The SEC file number for each of the documents listed above is 000-50626.

In addition, all reports and other documents filed by us pursuant to the Exchange Act after the date of the initial registration statement and prior to effectiveness of the registration statement shall be deemed to be incorporated by reference into this prospectus.

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You may request, orally or in writing, a copy of these filings, which will be provided to you at no cost, by writing or calling us at: 200 Connell Drive, Suite 1500, Berkeley Heights, NJ 07922, telephone (908) 517-7330. Information about us is also available at our website at http://www.cyclacel.com. However, the information in our website is not a part of this prospectus and is not incorporated by reference into this prospectus.

To the extent that any statements contained in a document incorporated by reference are modified or superseded by any statements contained in this prospectus, such statements shall not be deemed incorporated in this prospectus except as so modified or superseded.

All documents subsequently filed by us pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and prior to the termination of this offering are incorporated by reference and become a part of this prospectus from the date such documents are filed. Any statement contained in this prospectus or in a document incorporated by reference is modified or superseded for purposes of this prospectus to the extent that a statement contained in any subsequent filed document modifies or supersedes such statement.

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Cyclacel Pharmaceuticals, Inc.
Up to $4,000,000
Common Stock

Prospectus Supplement

June 23, 2016