Cyclacel Pharmaceuticals, Inc.
Form S-3/A
June 03, 2016
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As filed with the Securities and Exchange Commission on June 3, 2016
Registration No. 333-211046

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Pre-Effective Amendment No. 2
to
Form S-3
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

CYCLACEL PHARMACEUTICALS, INC.
(Exact name of registrant as specified in its charter)

Delaware	91-1707622
(State or other jurisdiction of incorporation or organization)	(IRS employer Identification number)

200 Connell Drive, Suite 1500
Berkeley Heights, NJ 07922
(908) 517-7330
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)
Spiro Rombotis
President and Chief Executive Officer
Cyclacel Pharmaceuticals, Inc.
200 Connell Drive, Suite 1500
Berkeley Heights, NJ 07922
(908) 517-7330
(Name, address, including zip code, and telephone number, including area code, of agent for service)

With a copy to:
Joel I. Papernik, Esq.
Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.
666 Third Avenue
New York, New York 10017
(212) 935-3000

Approximate date of commencement of proposed sale to the public: From time to time after this Registration Statement becomes effective.
If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box.

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

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

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	Accelerated filer	Non-accelerated filer (Do not check if a smaller reporting company)	Smaller reporting company

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CALCULATION OF REGISTRATION FEE

Title of each Class of Securities to be Registered(1)	Proposed Maximum Aggregate Offering Price(2)(3)	Amount of Registration Fee(4)
Common Stock, $0.001 par value per share	(5)	
Preferred Stock, $0.001 par value per share	(5)	
Warrants to purchase Common Stock	(5)	
Debt Securities	(5)	
Units	(5)	
Total	$ 100,000,000	$ 10,070(6)

(1)
There are being registered under this registration statement such indeterminate number of shares of common stock, shares of preferred stock, warrants to purchase common stock, debt securities, rights and purchase contracts to purchase common stock and a combination of such securities, separately or as units, as may be sold by the registrant from time to time, which collectively shall have an aggregate initial offering price not to exceed $100,000,000. If any debt securities are issued at an original issue discount, then the offering price of such debt securities shall be in such greater principal amount as shall result in an aggregate initial offering price not to exceed $100,000,000, less the aggregate dollar amount of all securities previously issued hereunder. Any securities registered hereunder may be sold separately or as units with other securities registered hereunder. The securities registered also include such indeterminate amounts and numbers of common stock as may be issued upon conversion of preferred stock or pursuant to the anti-dilution provisions of any such securities. The securities registered also include such indeterminate amounts and numbers of common stock as may be issued upon exercise of warrants or pursuant to the anti-dilution provisions of any such securities. The securities registered also include such indeterminate amounts and numbers of common stock and debt securities as may be issued upon conversion of or exchange for debt securities that provide for conversion or exchange, upon exercise of warrants or pursuant to the anti-dilution provisions of any such securities. In addition, pursuant to Rule 416 under the Securities Act of 1933, as amended (the “Securities Act”), the shares of common stock being registered hereunder include such indeterminate number of shares of common stock as may be issuable with respect to the shares being registered hereunder as a result of stock splits, stock dividends, or similar transactions.

(2)
The proposed maximum per unit and aggregate offering prices per class of security will be determined from time to time by the registrant in connection with the issuance by the registrant of the securities registered hereunder.

(3)
Estimated solely for purposes of determining the registration fee pursuant to Rule 457(o) under the Securities Act. The aggregate maximum offering price of all securities issued pursuant to this registration statement will not exceed $100,000,000.

(4)
Calculated pursuant to Rule 457(o) based on an estimate of the proposed maximum aggregate offering price.

(5)

Not required to be included in accordance with General Instruction II.D of Form S-3 and Rule 457(o) under the Securities Act.

(6)
Pursuant to Rule 457(p) under the Securities Act, the registrant hereby offsets the total registration fee due under this registration statement by the amount of the filing fee associated with the unsold primary securities from the registrant's Form S-3 Registration Statement, filed by the registrant with the Securities and Exchange Commission on April 8, 2013 and declared effective on April 22, 2013 (File No 333-187801), registering primary securities to be sold by the registrant for a maximum aggregate offering price of $75,000,000 (the "Prior Registration Statement"). Of that amount, the registrant sold securities for an aggregate offering price of $46,220,739, leaving a balance of unsold securities with an aggregate offering price of $28,779,261. The associated filing fee of $3,925.49 for such unsold securities, calculated under Rule 457(o), is hereby used to offset the current registration fee due. Accordingly, the full amount of the $10,070 registration fee currently due for this registration statement is being paid by (i) the offset against the balance of the fee paid for the Prior Registration Statement, and (ii) the current payment by the registrant of $6,144.51, of which the registrant paid $2,500 in connection with this registration statement when filed originally on April 29, 2016, and the balance of $3,644.51 when filed on May 2, 2016.

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until the registration statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

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The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and is not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED JUNE 3, 2016

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 2, 2016, the last reported sale price of our common stock was $4.58 per share, and the last reported sale price of our preferred stock was $4.45 per share.

The aggregate market value of our outstanding shares of common stock held by non-affiliates was $11,781,202.70 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 $4.58 based on the closing sale price of our common stock on the NASDAQ Capital Market on June 2, 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 , 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 ou