Cyclacel Pharmaceuticals, Inc.
Form 10-K
March 29, 2010

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**UNITED STATES**
**SECURITIES AND EXCHANGE COMMISSION**
**Washington, D.C. 20549**
**FORM 10-K**

(Mark One)

þ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
**FOR THE FISCAL YEAR ENDED DECEMBER 31, 2009**

**OR**

o **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

**Commission file number 00-50626**

**CYCLACEL PHARMACEUTICALS, INC.**

(Exact name of registrant as specified in its charter)

| Delaware | 91-1707622 |
|---|---|
| (State or Other Jurisdiction of Incorporation or Organization) | (I.R.S. Employer Identification No.) |
| 200 Connell Drive Suite 1500, Berkeley Heights, New Jersey | 07922 |
| (Address of principal executive offices) | (Zip Code) |

Registrant s telephone number, including area code: (908) 517-7330

Securities registered under Section 12(b) of the Exchange Act:

| **Title of Each Class** | **Name of Each Exchange on Which Registered** |
|---|---|
| Common Stock, $0.001 par value | The NASDAQ Stock Market LLC |
| Preferred Stock, $0.001 par value | The NASDAQ Stock Market LLC |

Securities registered pursuant to Section 12(g) of the Act: None.

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes o No þ

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange Act. Yes o No þ

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes þ No o

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to

submit and post such files). Yes o No o

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S- K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendments to this Form 10-K. þ

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 o | Accelerated filer o | Non-accelerated filer o [Do not check if a smaller reporting company] | Smaller reporting company þ |
|---|---|---|---|

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes o No þ

The aggregate market value of the registrant s voting and non-voting common stock held by non-affiliates of the registrant (without admitting that any person whose shares are not included in such calculation is an affiliate), as of June 30, 2009 (based upon the closing sale price of $1.13 of such shares on The NASDAQ Global Market on June 30, 2009) was $19,164,232.

As of March 26, 2010, there were 35,411,325 shares of the registrant s common stock outstanding.

**DOCUMENTS INCORPORATED BY REFERENCE**

The following documents (or parts thereof) are incorporated by reference into the following parts of this Annual Report on Form 10-K: Certain information required in Part III of this Annual Report on Form 10-K is incorporated from the registrant s Proxy Statement relating to the 2010 Annual Meeting of Stockholders, to be held on May 25, 2010, which we will file with the Securities and Exchange Commission within 120 days after our December 31, 2009 fiscal year end.

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## PART I

### Item 1. Business

In this report, Cyclacel, the Company, we, us, and our refer to Cyclacel Pharmaceuticals, Inc.

**General**

Cyclacel Pharmaceuticals, Inc. was incorporated in the state of Delaware in 1996 and is headquartered in Berkeley Heights, New Jersey, with a research facility located in Dundee, Scotland. Cyclacel is a development stage biopharmaceutical company dedicated to the discovery, development and commercialization of novel, mechanism-targeted drugs to treat human cancers and other serious disorders. Cyclacel s strategy is to build a diversified biopharmaceutical business focused in hematology and oncology based on a portfolio of commercial products and a development pipeline of novel drug candidates. As a development stage enterprise, substantially all efforts of the Company to date have been devoted to performing research and development, conducting clinical trials, developing and acquiring intellectual property, raising capital and recruiting and training personnel.

**Recent Developments**

On January 27, 2010, we announced that The NASDAQ Global Market, or NASDAQ, had notified us that we regained compliance with the minimum $50 million market value of listed securities requirement and that we currently comply with all other applicable standards for continued listing on NASDAQ.

On January 25, 2010, we completed the sale of 2,350,000 units in a registered direct offering at a purchase price of $2.50 per unit to certain institutional investors of the Company for gross proceeds of approximately $5.9 million. Each unit consisted of one share of our common stock and one warrant to purchase 0.30 of one share of our common stock. The warrants have a five-year term from the date of issuance, are exercisable beginning six months from the date of issuance and will be exercisable at an exercise price of $2.85 per share of common stock.

On January 13, 2010, we completed the sale of 2,850,000 units in a registered direct offering to certain institutional investors. Each unit was sold at a purchase price of $2.51 per unit and consists of one share of our common stock and one warrant to purchase 0.25 of one share of our common stock for gross proceeds of approximately $7.2 million. The warrants have a five-year term from the date of issuance, are exercisable beginning six months from the date of issuance and will be exercisable at an exercise price of $3.26 per share of common stock.

On January 7, 2010, our Board decided not to declare the quarterly cash dividend on the Company s 6% Convertible Exchangeable Preferred Stock, or Preferred Stock, with respect to the fourth quarter of 2009 that would have otherwise been payable on February 1, 2010. As previously disclosed, the Board also did not declare the quarterly cash dividend with respect to the first, second and third quarters of 2009. To the extent that any dividends payable on the Preferred Stock are not paid, such unpaid dividends are accrued. This is the fourth quarterly dividend the Company decided not to declare and if we fail to pay dividends for at least six quarters (whether or not consecutive) on the Preferred Stock, the size of our Board of Directors could be increased by two members and the holders of the Preferred Stock, voting separately as a class, will have the right to vote to fill the two vacancies created thereby until all accrued but unpaid dividends have been paid in full, at which time such right is terminated.

Through March 25, 2010, we issued 2,618,266 shares of our common stock for gross proceeds of approximately $2.6 million through the exercise of warrants. In addition, we completed draw downs from our Committed Equity financing Facility, or CEFF, under which we issued 1,563,208 shares for proceeds of approximately $3.1 million.

During March 2010, we issued 239,396 shares of our common stock to a stockholder in exchange for the stockholder s delivery to us of 123,400 shares of our outstanding Preferred Stock.

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**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.

**Overview**

We are a biopharmaceutical business dedicated to the discovery, development and commercialization of novel, mechanism-targeted drugs to treat cancer and other serious disorders. We are focused on delivering leading edge therapeutic management of cancer patients based on a clinical development pipeline of novel drug candidates. Our core area of expertise, and a foundation of the Company since our inception, is in cell cycle biology; the processes by which cells divide and multiply. 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.

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

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

We have additional clinical programs which are currently pending availability of clinical data. Once data become available and are reviewed, we will determine the feasibility of pursuing further development and/or partnering these assets including sapacitabine in combination with seliciclib, seliciclib in NSCLC and nasopharyngeal cancer, or NPC, and CYC116. In addition, we market directly in the United States Xclair® Cream for radiation dermatitis and Numoisyn® Liquid and Numoisyn® Lozenges for xerostomia.

We were founded by Professor Sir David Lane, a recognized leader in the field of tumor suppressor biology who discovered the p53 protein, which operates as one of the body s own anticancer agents by regulating cell cycle targets. Our Chief Scientist, Professor David Glover, is a recognized leader in the biology of mitosis or cell division. Professor Glover discovered, among other cell cycle targets, the mitotic kinases, Polo and Aurora, enzymes that act in the mitosis phase of the cell cycle.

Although our resources are primarily directed towards advancing our anticancer drug candidate sapacitabine through in-house development activities we are also progressing, but with lower levels of investment than in previous years, our other novel drug series which are at earlier stages. Taken together, our pipeline covers all four phases of the cell cycle, which we believe will improve the chances of successfully developing and commercializing novel drugs that work on their own or in combination with approved conventional chemotherapies or with other targeted drugs to treat human cancers. As a consequence of our focus on sapacitabine clinical development and related cost reduction program, research and development expenditures for the year ended December 31, 2009 were reduced by $9.1 million, or 48%, to $9.8 million compared to $18.9 million for the year ended December 31, 2008.

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We have executed our strategy through the following activities:

***Advancing our research and development programs***

Submitted a Special Protocol Agreement, or SPA, to the U.S. Food and Drug Administration, or FDA, for a randomized Phase 3 study design for sapacitabine in elderly AML following a Type A meeting with the FDA in December 2009;

Cyclacel s cyclin dependent kinase, or CDK, inhibitors mechanism of action, target profile and selectivity elucidated in recent publications which reported activity in highly transformed and/or resistant cancers and potential in other proliferative diseases;

Sapacitabine Phase 2 elderly AML trial 1-year survival data announced at the 2009 American Society of Hematology (ASH) annual meeting;

Sapacitabine Phase 2 trial of patients with MDS interim results announced at the 2009 ASH annual meeting;

Sapacitabine and seliciclib combination trial initiated Phase 1 trial for solid tumors; and

Seliciclib Phase 2 trial of NPC initial results reported at the 2009 American Society of Clinical Operations, or ASCO, meeting.

***Managing our resources***

Ended 2009 with approximately $11.5 million of cash and cash equivalents and short-term investments. Raised an additional $15.6 million in gross proceeds through two registered direct offerings in January 2010 and the exercise of warrants;

In November 2009, we amended the Kingsbridge Capital Limited Committed Equity Financing Facility and raised approximately $1.0 million;

In July 2009, we raised $3.4 million in gross proceeds through a registered direct offering; and

Followed our operating plan with the focus on sapacitabine clinical development and further lowered operating costs through a reduction in workforce in the second and third quarters of 2009; since announcing our revised operating plan in September 2008, we have reduced our workforce by fifty one (51) people, or 63% of our workforce and closed our Cambridge research facility.

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***Research and Development Pipeline***

The following table summarizes our clinical and preclinical programs.

| Program | Indication | Development Status | Target | Cell Cycle Mechanism |
|---|---|---|---|---|
| *Oncology* | | | | |
| Sapacitabine, CYC682 | Elderly AML | Phase 2 randomized trial completed | DNA polymerase | G2 and S phase |
| Sapacitabine, CYC682 | MDS | Phase 2 randomized trial on-going | DNA polymerase | G2 and S phase |
| Sapacitabine, CYC682 | CTCL | Phase 2 randomized trial stopped. Not a company priority | DNA polymerase | G2 and S phase |
| Sapacitabine, CYC682 | NSCLC | Phase 2 trial on-going | DNA polymerase | G2 and S phase |
| Sapacitabine + Seliciclib | Cancer | Phase 1 trial on-going | | |
| Seliciclib, CYC202 | NSCLC | Phase 2b randomized trial closed to accrual | CDK2/A, 2/E, 7, 9 | G1/S checkpoint and others |
| Seliciclib, CYC202 | NPC | Phase 2 randomized trial. Lead-in phase only on-going | CDK2/A, 2/E, 7, 9 | G1/S checkpoint and others |
| CYC116 | Cancer | Phase 1 trial completed | Aurora kinase & VEGFR2 | Mitosis |
| CDK Inhibitors, Second Generation | Cancer | Preclinical | CDK | G1/S checkpoint and others |
| Plk1 Inhibitors | Cancer | Preclinical | Plk | G2/M checkpoint |
| Hdm2 Inhibitors | Cancer | On hold, Not a company priority | Hdm2 | G1/2 phase |
| Cyclin Binding Groove Inhibitors | Cancer | On hold. Not a company priority | Cyclin binding groove | S phase |
| *Other therapeutic areas* | | | | |
| Cell Cycle Inhibitors | Autoimmune & Inflammatory Diseases | Phase 1 trial completed On hold. Not a company priority | CDK | G1/S checkpoint and others |
| Cell Cycle Inhibitors | HIV/AIDS | On hold. Not a company priority | CDK | Other |
| GSK-3 Inhibitors | Type 2 Diabetes | On hold. Not a company priority | GSK-3 | Other |

***Market opportunity in oncology***

Cancer remains a major life-threatening disease in the United States with approximately 3.2 million people afflicted by cancer and approximately 1.4 million new cases of cancer diagnosed every year. Five common solid cancer types: non-small cell lung, breast, ovarian, prostate and colorectal cancers, represent over 50% of all new cases of cancer in

the United States each year and account for more than 50% of all cancer deaths in the United States.
Acute myeloid leukemia is one of the most common types of leukemia or cancer in the blood and bone marrow. According to the American Cancer Society approximately 44,000 cases of leukemia are diagnosed annually in the United States of which about 13,000 are classified as AML. Leukemia is a deadly disease with an estimated 9,000 deaths annually in the United States, almost all in adults. The average age of a patient with AML is 67 and about two-thirds of AML patients are above 60 years old. The prognosis of AML in the elderly is poor.

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There are approximately 11,000 new cases of myelodysplastic syndromes diagnosed annually in the United Sates with incidence rates between 16,000 and 20,000. Patients currently receive hypomethylating agents as first-line treatment and while survival rates exceed one year, there is no established therapy for second-line treatment.

Lung cancer is a cancer starting in the lungs that often takes many years to develop. About 85% to 90% of all lung cancers are of NSCLC type. According to the American Cancer Society, an estimated 215,000 patients are diagnosed annually with NSCLC in the United States. An estimated 380,000 new cases are diagnosed annually in the European Union. NSCLC is a deadly disease with an estimated 162,000 deaths annually in the United States.

NPC develops in the nasopharynx, an area in the back of the nose toward the base of the skull. Although it is sometimes considered a head and neck or an oral cancer, nasopharyngeal cancer is different from these cancers. It is frequently fatal, once the disease recurs after initial chemotherapy and radiotherapy, spreads widely and has different risk factors such as Epstein-Barr virus, or EBV infection. High EBV viral titers are considered an indicator of poor prognosis. According to the American Cancer Society, an estimated 2,100 patients are diagnosed annually with nasopharyngeal cancer in the United States. An estimated 2,500 are diagnosed annually in the European Union, but an estimated 70,000 new cases are diagnosed annually in the Asia Pacific region.

Lymphoma is a cancer of lymphoid tissue, a part of the lymphatic system. Lymphoid tissue is formed by several types of immune system cells that work together mainly to resist infections. About 5% of all lymphomas start in the skin often staying there without spreading to internal organs and are called cutaneous lymphomas. The main cell types found in lymphoid tissue are B lymphocytes and T lymphocytes resulting in B-cell or T-cell lymphoma, or CTCL. CTCL causes disfiguring skin lesions and severe itching. According to the American Cancer Society, an estimated 3,000 patients are diagnosed annually with lymphoma in the skin in the United States.

***Oncology Development Programs***

We are generating several families of anticancer drugs that act on the cell cycle, including nucleoside analogues, cyclin dependent kinase, or CDK, inhibitors and Aurora kinase/Vascular Endothelial Growth Factor Receptor 2, or AK/VEGFR2 inhibitors. Although a number of pharmaceutical and biotechnology companies are currently attempting to develop nucleoside analogues, CDK inhibitor, AK and/or VEGFR inhibitor drugs, we believe that our drug candidates, are differentiated in that they are orally available and interact with unique target profiles and mechanisms. For example we believe that our sapacitabine is the only orally available nucleoside analogue presently being tested in Phase 2 trials in AML, and seliciclib is the only orally available CDK inhibitor currently in Phase 2 trials.

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

Our approach to drug discovery and development has relied on proprietary genomic technology to identify gene targets, which are then progressed by means of structure-based drug design techniques through to the development stage. This approach is exemplified by our Aurora kinase, or AK, and Polo-like kinase, or Plk, inhibitor programs. Fundamentally, this approach to drug discovery and design aims to improve our ability to select promising drug targets in the early stages of the process so as to decrease compound attrition rates during the later, more expensive stages of drug development. By devoting resources initially to this process, we were able to focus our efforts on targets that have a higher probability of yielding successful drug candidates through the utilization of an integrated suite of sophisticated discovery and design technologies by highly skilled personnel. However, as a result of the reduction in our workforce in 2008 and 2009 our ability to identify, optimize and develop new targets is significantly curtailed.

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***Sapacitabine***

Our lead candidate, sapacitabine, is an orally available prodrug of CNDAC, which is a novel nucleoside analog, or a compound with a structure similar to a nucleoside. A prodrug is a compound that has a therapeutic effect after it is metabolized within the body. CNDAC has a significantly longer residence time in the blood when it is produced in the body through metabolism of sapacitabine than when it is given directly. Sapacitabine acts through a dual mechanism whereby the compound interferes with DNA synthesis and repair by causing single-strand DNA breaks and induces arrest of the cell division cycle at G2/M checkpoint. A number of nucleoside drugs, such as gemcitabine, or Gemzar®, from Eli Lilly, and cytarabine, also known as Ara-C, a generic drug, are in wide use as conventional chemotherapies. Both sapacitabine and its major metabolite, CNDAC, have demonstrated potent anti-tumor activity in both blood and solid tumors in preclinical studies. In a liver metastatic mouse model, sapacitabine was shown to be superior to gemcitabine and 5-FU, two widely used nucleoside analogs, in delaying the onset and growth of liver metastasis. We have retained worldwide rights to commercialize sapacitabine, except for Japan, for which Daiichi-Sankyo Co., Ltd, or Daiichi-Sankyo, has a right of first negotiation.

We are currently exploring sapacitabine in both hematological cancers and solid tumors. To date, sapacitabine has been evaluated in approximately 400 patients in several Phase 1 and 2 studies and has shown signs of anti-cancer activity.

*Hematological Cancers*

*Phase 1 clinical trial in patients with advanced leukemias and myelodysplastic syndromes*

In December 2007, at the ASH annual meeting, we reported interim results from a Phase 1 clinical trial of oral sapacitabine in patients with advanced leukemias and MDS. The data demonstrated that sapacitabine had a favorable safety profile and promising anti-leukemic activity in patients with relapsed and refractory AML and MDS when administered by two different dosing schedules. The primary objective of the study is to determine the maximum tolerated dose, or MTD, of sapacitabine administered twice daily for seven consecutive days every 21 days or three consecutive days per week for two weeks every 21 days. The MTD was reached at 375 mg on the seven-day schedule and 475 mg on the three-day schedule. Dose-limiting toxicity was gastrointestinal which included abdominal pain, diarrhea, small bowel obstruction and neutropenic colitis. One patient treated at the MTD of 375 mg on the seven-day schedule died of complications from neutropenic colitis. Among 46 patients, 42 with AML and 4 with MDS, in this dose escalating study, the best responses were complete remission, or CR, or complete remission without platelet recovery, or CRp, in six patients for an Overall Response Rate of 13%. In addition, 15 patients had a significant decrease in bone marrow blasts including seven with blast reduction to 5% or less. The study was conducted at The University of Texas M. D. Anderson Cancer Center and is led by Hagop Kantarjian, M.D., Professor of Medicine and Chairman of the Leukemia Department and Dr. William Plunkett, Professor and Chief, Section of Molecular and Cellular Oncology, Department of Experimental Therapeutics.

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

In December 2007, we initiated an open-label, multicenter, randomized Phase 2 clinical trial of oral sapacitabine in 60 elderly patients with AML aged 70 or older who are previously untreated or in first relapse. The Phase 2 study, led by Dr. Kantarjian, has a primary endpoint of 1-year survival rate of three dosing schedules of sapacitabine in elderly patients with previously untreated or first relapsed AML. Secondary objectives are to assess CR or CRp, partial remission, or PR, duration of CR or CRp, or major hematological improvement and their corresponding durations, transfusion requirements, number of hospitalized days and safety. The study uses a selection design with the objective of identifying a dosing schedule among three different arms, A. 200 mg twice daily for seven days every 3-4 weeks, B. 300 mg twice daily for seven days every 3-4 weeks, and C. 400 mg twice daily for three days per week for two weeks every 3-4 weeks, which produces a better 1-year survival rate in the event that all three dosing schedules are active. Each arm enrolled and treated 20 patients. Approximately 55% of patients had AML de novo and the rest had AML preceded by antecedent hematological disorder, or AHD, such as MDS, or myeloproliferative disease. Eighty percent of the patients were untreated and 20% in first relapse. We completed enrollment of 60 AML patients in this study in October 2008. In December 2009, at the 51st Annual Meeting of ASH we reported 1-year survival data.

The primary endpoint of 1-year survival was 35% on Arm A, 30% on Arm C and 10% on Arm B. The median overall survival was 212 days on Arm C (range of 13 to over 654 days), 197 days on Arm A (range of 26 to over 610 days) and 100 days on Arm B (range of 6 to over 646 days). Overall response rate, or ORR, a secondary endpoint, was 45% on Arm A, 35% on Arm C and 25% on Arm B with CR rate of 25% on Arm C and 10% on Arms A and B. Thirty-day mortality was 10% on Arm C and Arm A and 20% on Arm B. Approximately 30% of all patients received sapacitabine for at least 6 cycles. Fifteen patients who survived one year or more received an average of 12 treatment cycles.

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

The 3-day dosing schedule in Arm C was selected for further clinical development in elderly patients with de novo AML based on a 1-year survival rate of 30%, ORR of 35% with durable CRs. The 7-day dosing schedule in Arm A was selected for further clinical development in elderly patients with AML preceded by AHD based on a 1-year survival rate of 35%, ORR of 45% with durable hematological improvement.

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

In September 2008, we advanced sapacitabine into Phase 2 development as a second-line treatment in patients aged 60 or older with MDS who are previously treated with hypomethylating agents. The MDS stratum of the study is designed as a protocol amendment expanding the ongoing Phase 2 trial of sapacitabine in AML described above, to include a cohort of patients with MDS. Patients with MDS often progress to AML. The primary objective of the MDS stratum is to evaluate the 1-year survival rate of three dosing schedules of sapacitabine. 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. The study uses a selection design with the objective of identifying a dosing schedule which produces a better 1-year survival rate for each stratum in the event that all three dosing schedules are active.

In December 2009, at the 51st ASH Annual Meeting, we reported interim response data for the ongoing Phase 2 clinical trial of sapacitabine in older patients with MDS. The study has recently completed enrollment of 60 patients aged 60 or older with MDS who were previously treated with azacitidine and/or decitabine. Each arm enrolled 20 patients randomized across the same three dosing schedules of sapacitabine (Arms A, B and C) tested in the AML stratum of the study. Forty-nine of the patients enrolled have been followed-up for more than 30 days. Approximately 46% of the 49 patients had baseline bone marrow blast counts above 10%. Based on interim data, the highest number of responses was observed on Arm B, the 7-day high dose schedule. Thirty-day mortality from all-causes is 8.2%. Approximately 30% of the patients received 4 or more cycles of sapacitabine.

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*Pivotal trial plan for sapacitabine for the treatment of hematological malignancies*

In December 2009, we announced that we held a Type A meeting with the FDA to discuss a randomized Phase 3 study design for our oral sapacitabine capsules in AML and separately in MDS. Based on the FDA s confirmation that the proposed study design would be acceptable for a SPA, we submitted a SPA request during the first quarter of 2010. Should the SPA be granted we would plan to start such a study during 2010. The SPA process allows for official FDA evaluation of clinical protocols of a Phase 3 clinical trial intended to form the primary basis for an efficacy claim. A SPA provides trial sponsors with an FDA agreement that the design and analysis of the trial adequately address objectives in support of a submission for a marketing application if the trial is performed according to the SPA. The SPA may only be changed through a written agreement between the sponsor and the FDA, or if the FDA becomes aware of a substantial scientific issue essential to product efficacy or safety. However, a SPA does not provide any assurance that a marketing application would be approved by the FDA. Furthermore, Phase 3 clinical trials are time-consuming and expensive, and because we have limited resources, we may be required to collaborate with a third party or raise additional funds. However, there is no assurance that we will be able to do so.

***Solid Tumors***

*Phase 1 clinical trials in patients with refractory solid tumors or lymphomas*

Two Phase 1 studies of sapacitabine were completed by Daiichi-Sankyo, from which we in-licensed sapacitabine, evaluating 87 patients in refractory solid tumors. In addition, we conducted a Phase 1b dose escalation clinical trial in patients with refractory solid tumors or lymphomas. Preliminary results of the Phase 1b study were reported at the EORTC-NCI-AACR Molecular Targets and Cancer Therapeutics meeting in November 2006. The primary objective of the study was to evaluate the safety profile of sapacitabine administered twice daily for 14 consecutive days or 7 consecutive days every 21 days. Of the 37 treated patients, 28 received the drug twice daily for 14 days and 9 received the drug twice daily for 7 days. The dose-limiting toxicity was reversible myelosuppression. One patient treated at the maximum tolerated dose died of candida sepsis in the setting of grade 4 neutropenia and thrombocytopenia. Non-hematological toxicities were mostly mild to moderate. The best response by investigator assessment was stable disease in 13 patients, five with non-small cell lung cancer, two with breast cancer, two with ovarian cancer and one each with colorectal cancer, adenocarcinoma of unknown primary, gastrointestinal stromal tumor, and parotid acinar carcinoma.

*Phase 2 clinical trial in patients with non-small cell lung cancer*

In January 2009, we began treating patients in a Phase 2, open label, single arm, multicenter clinical trial in patients with NSCLC who have had one prior chemotherapy. This study builds on the observation of prolonged stable disease of four months or longer experienced by heavily pretreated NSCLC patients involved in two Phase 1 studies of sapacitabine. The multicenter Phase 2 trial is led by Philip D. Bonomi, M.D., at Rush University Medical Center, Chicago. The primary objective of the study is to evaluate the rate of response and stable disease in patients with previously treated NSCLC. Secondary objectives are to assess progression-free survival, duration of response, duration of stable disease, 1-year survival, overall survival and safety. The study will enroll approximately 40 patients and has a lead-in phase for dose escalation with the objective of defining a recommended dose followed by a second stage in which patients will be treated at the recommended dose.

*Phase 2 clinical trial in patients with cutaneous T-cell lymphoma, or CTCL*

In April 2007, we initiated a Phase 2 clinical trial in patients with advanced CTCL, a cancer of T-lymphocytes, or white blood cells, which causes disfiguring skin lesions and severe itching. The primary objective of the study is to evaluate tolerability and response rate of 50 mg and 100 mg regimens of sapacitabine both twice a day for three days per week for two weeks in a three week cycle in patients with progressive, recurrent, or persistent CTCL on or following two systemic therapies. The study uses a selection design to choose an optimal dose if both are active. Secondary objectives are to assess response duration, time to response, time to progression and relief of pruritus or itching. Non-hematological toxicities were mostly mild to moderate. The best response by investigator assessment was partial response in 3 patients out of 16 enrolled. We stopped the trial in order to re-direct our resources to sapacitabine clinical trials with a higher priority.

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*EU Orphan Designation*

During May 2008, we received designation from the European Medicines Evaluation Agency, or EMEA, for sapacitabine as an orphan medicine in two separate indications: AML and MDS. The EMEA s Committee for Orphan Medicinal Products, or COMP, adopted a positive opinion on the Company s 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, EMEA scientific advice on protocol development, direct access to the centralized procedure for review of marketing authorizations, EMEA fee reductions and eligibility for grant support from European agencies.

***Seliciclib***

Our second drug candidate, seliciclib, is a novel, first-in-class, orally available, CDK inhibitor. The compound selectively inhibits a spectrum of enzyme targets -CDK2/E, CDK2/A, CDK7 and CDK9- that are central to the process of cell division and cell cycle control. The target profile of seliciclib is differentiated from the published target profile of other CDK inhibitors. Its selectivity is differentiated by recent publications by independent investigators which showed that seliciclib (i) is more active against NSCLC cells with K-Ras or N-Ras mutations than those with wild type Ras and (ii) overcomes resistance to letrozole (Femara®) in breast cancer cells caused by a particular form of cyclin E in complex with CDK2. Preclinical studies have shown that the drug works by inducing cell apoptosis, or cell suicide, in multiple phases of the cell cycle. To date, seliciclib has been evaluated in approximately 450 patients in several Phase 1 and 2 studies and has shown signs of anti-cancer activity. We have retained worldwide rights to commercialize seliciclib.

*Phase 1 clinical trials in patients with refractory solid tumors*

We have completed two Phase 1 trials that enrolled 24 healthy volunteers and three Phase 1 trials that enrolled a total of 84 cancer patients testing different doses and schedules. The primary toxicities observed were of a non-hematological nature, including asthenia or weakness, elevation of liver enzymes, hypokalemia or decreased potassium levels, nausea and vomiting and elevation in creatinine. Although these trials were designed to test safety rather than efficacy of seliciclib given alone as monotherapy in patients with solid tumors who failed multiple previous treatments, several of these patients appeared to have benefited from seliciclib treatment.

Seliciclib was shown in a further Phase 1 study sponsored and conducted by independent investigators to have clinical antitumor activity in patients with nasopharyngeal cancer, measured as a decrease in the size of primary tumor and involved lymph nodes, as well as an increase in tumor cell deaths by biomarker analyses.

*Phase 2 clinical trials in patients with NSCLC or breast cancer*

Four Phase 2 trials have been conducted in cancer patients to evaluate the tolerability and antitumor activities of seliciclib alone or in combination with standard chemotherapies used in the treatment of advanced NSCLC or breast cancer. Interim data from two Phase 2 open-label studies of a total of 52 patients with NSCLC, suggest that seliciclib treatment did not aggravate the known toxicities of standard first and second-line chemotherapies nor appear to cause unexpected toxicities, although these trials were not designed to provide statistically significant comparisons. The combination of seliciclib with a standard dose of Capecitabine (Xeloda®) was not well tolerated in patients with advanced breast cancer.

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Seliciclib is currently being investigated in the Phase 2b APPRAISE study as a treatment for patients with advanced NSCLC. APPRAISE is a double-blinded, randomized study of single agent seliciclib versus best supportive care in patients with NSCLC treated with at least two prior systemic therapies. APPRAISE is led by Chandra P. Belani, M.D. at Milton S. Hershey Medical Center, Penn State University. The study s main objective is to learn the anti-tumor activity of seliciclib as a single agent in refractory NSCLC and help determine further development strategies. The study design is randomized discontinuation. All patients receive seliciclib at a dose of 1200 mg twice a day for three days for at least three cycles of two weeks each. Patients who achieve stable disease after three cycles will be randomized to continue on seliciclib or receive placebo with best supportive care. Patients in the placebo arm who progress will be given the option to cross-over and again receive seliciclib. The primary efficacy endpoint of APPRAISE is doubling progression free survival, or PFS, measured in the randomized portion of the study.

In August 2008, we announced that an independent data review committee, or IDRC, completed a review of the first interim analysis data from the study. The IDRC assessed the safety profile of seliciclib and recommended that the study continue after reviewing data from 173 patients with previously-treated NSCLC, of whom 45 proceeded into the blinded portion of the study and were randomized to receive either seliciclib or best supportive care. Based on the interim data, the IDRC reached the following main conclusions: there were no safety concerns that would warrant stopping the study; there was no trend favoring the seliciclib treatment arm; and as a definitive conclusion could not be reached because of the low number of events, it was recommended that the study be continued. Based on our cost versus benefit analysis, we decided not to enroll additional patients. The APPRAISE trial continues with the 191 patients already enrolled until the last enrolled patient has completed follow-up. In accordance with the protocol, we remain blinded to the study data.

*Phase 2 clinical trials in patients with NPC*

In November 2007, we commenced a Phase 2 multicenter, international, blinded randomized study of oral seliciclib as a single agent in patients with NPC. The primary objective is to evaluate 6-month progression free survival, or PFS, of two dosing schedules of seliciclib in approximately 75 patients with previously treated NPC. Secondary objectives are overall survival, response rate, response duration, safety and tolerability. The first part of the study is designed to confirm safety and tolerability of 400 mg twice a day for four days per week or 800 mg once a day for four days per week of seliciclib. It is open to approximately 12 to 24 patients with advanced solid tumors as well as patients with NPC. The second part of the study is designed to detect major differences between the two dosing schedules of seliciclib and a placebo group in terms of 6-month PFS in approximately 51 patients. The start of the second part of the study is dependent on clinical data from the lead-in phase and available resources.

In May 2009, at the ASCO annual meeting, we reported interim data from the lead-in portion of the Phase 2 study which demonstrated that oral seliciclib could be safely administered in two dosing schedules which were well tolerated and met the criteria for proceeding to the randomized stage of the study. Seliciclib treatment resulted in prolonged stable disease in 70% of previously-treated NPC patients, including 3 with stable disease lasting longer than 8 months, suggesting seliciclib inhibits tumor growth in NPC. The data support further clinical development of oral seliciclib in NPC.

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***CYC116***

In June 2007, we initiated 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. The multicenter Phase 1 trial, now completed, is designed to examine the safety and tolerability of CYC116 in patients with advanced solid tumors. The primary objective of the study is to determine the maximum tolerated dose. Secondary objectives are to evaluate pharmacokinetic and pharmacodynamic effects of the drug and document anti-tumor activity. Aurora kinases, or AK, are a family of serine/threonine protein kinases discovered by Professor David Glover, our Chief Scientist, that are only expressed in actively dividing cells and are crucial for the process of cell division or mitosis. These proteins, which have been found to be over-expressed in many types of cancer, have generated significant scientific and commercial interest as cancer drug targets. VEGFR2 is a receptor protein that plays a key regulatory role in the angiogenesis pathway, or blood vessel formation. VEGFR is targeted by recently approved drugs such as bevacizumab and sorafenib indicated for the treatment of several solid cancers, such as breast, colorectal, kidney, liver and lung. We have retained worldwide rights to commercialize CYC116. Further work on CYC116 will be undertaken when appropriate levels of resource are available to direct to the program.

***Other programs***

We have allocated limited resources to other programs allowing us to maintain and build on our core competency in cell cycle biology and related drug discovery. In our second generation CDK inhibitor program, we have discovered several series of CDK inhibitors that we believe may prove to be more potent anticancer agents than seliciclib based on preclinical observations. Our polo-like kinase or Plk inhibitor program targets the mitotic phase of the cell cycle with the objective of identifying potent and selective small molecule inhibitors of Plk1, a kinase active during mitosis. Plk was discovered by Professor David Glover, our Chief Scientist. The Company has a number of earlier stage programs for which limited or no resources will be allocated. For example, extensive preclinical data published by independent investigators evidence activity by our CDK inhibitors, including seliciclib, in various autoimmune and inflammatory diseases of aberrant cell proliferation including glaucoma, lupus nephritis, idiopathic pulmonary fibrosis, polycystic kidney disease, and rheumatoid arthritis. In our GSK-3 inhibitor program we have demonstrated evidence of activity in preclinical models of Type 2 Diabetes.

Where appropriate we intend to progress such programs through collaboration with groups that specialize in the particular mechanism of action or disease area until such times that these programs can be partnered and/or progressed should funding become available. Where appropriate, the same approach will be used to progress unfunded programs described below.

***Hdm2 Inhibitors***

One of the key cell cycle regulatory proteins is p53, a protein discovered by our founder, Professor Sir David Lane. When active, p53 causes cell arrest at the G1/S checkpoint, inducing apoptosis in cancer cells. Under normal circumstances, p53 is held in an inactive form by binding to another regulatory protein, Hdm2. In this program, we have investigated ways of disrupting the interaction between Hdm2 and p53, thus activating p53. Through virtual screening technologies, we have identified two small molecule groups capable of breaking the binding between p53 and Hdm2.

***Cyclin Binding Groove Inhibitors***

The activity of CDK can be inhibited by various methods, such as by blocking the ATP site, as is the case with seliciclib, or by inhibiting the substrate binding site on the associated cyclin protein. Preventing cyclin A from binding to its substrates results in cell cycle arrest and induces apoptosis in cancer cells. This was the subject of a two-year collaboration with AstraZeneca that concluded in mid-2003. We have retained all intellectual property rights associated with this program.

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**Non-oncology Programs**

***Cell Cycle Inhibitors in Autoimmune & Inflammatory Diseases***

Preclinical results from several independent investigators suggest that cell cycle inhibitors such as seliciclib and its backup molecules arrest the progress of the cell cycle and may have therapeutic benefit in the treatment of patients with autoimmune and inflammatory diseases and in particular diseases characterized by uncontrolled cell proliferation. Published data indicate potential benefit in asthma, idiopathic pulmonary fibrosis, glomerulonephritis, lupus nephritis, polycystic kidney disease and rheumatoid arthritis.

***CDK Inhibitors in Virology***

Cell cycle inhibitors may be useful in the treatment of viral diseases to the extent that drugs can be developed that prevent the replication of virus in infected host cells and may inhibit their replication while sparing most uninfected cells. If this is proven in humans, cell cycle inhibitors may have significant potential in this area, as they do not rely on viral targets and are less likely to induce viral resistance, a major cause of failure of currently available antiviral drugs. We have investigated a number of compounds in this program, some of which appear to reduce HIV levels in biological tests with antiviral potency equivalent to some existing HIV/AIDS therapeutic agents. We intend to progress this program through collaboration with groups that specialize in virology research.

***GSK-3 Inhibitors in Type 2 Diabetes***

Inhibition of Glycogen Synthase Kinase-3 or GSK-3 is an essential element in the body s regulation of blood sugar. GSK-3 regulates the glycogen synthase enzyme that indirectly controls glucose levels. In healthy humans insulin controls the regulation of energy conversion and storage by interacting with its receptor which results in the activation of PI-3 kinase that in turn inhibits GSK-3. In patients with adult onset or Type 2 Diabetes GSK-3 inhibition does not occur resulting in failure of glucose control and the energy storage mechanism. We believe that GSK-3 inhibitor drugs may be suitable for development as Type 2 Diabetes therapies. GSK-3 is a target that is structurally very similar to CDK. We have identified four chemical families of GSK-3 inhibitors some of which are potent at picomolar concentrations which we believe are among the most potent GSK-3 inhibitors disclosed in relevant research literature. We have selected two lead compounds from the series, both of which have achieved proof-of-concept in the standard Zucker rat model of diabetes, demonstrating stimulation of glycogen synthase, improvement in glucose tolerance and regulation of triglycerides. We intend to progress this program through collaboration with groups that specialize in diabetes research.

**Commercial Products**

We have exclusive rights to sell and distribute three products in the United States and Canada used primarily to manage the effects of radiation or chemotherapy in cancer patients: Xclair® Cream, Numoisyn® Liquid and Numoisyn® Lozenges. All three products are approved in the United States under FDA 510 (k) or medical device registrations.

***Xclair® Cream***

Xclair® is an aqueous cream containing sodium hyaluronate, or hyaluronic acid, and glycyrrhetinic acid that is formulated to relieve symptoms associated with radiation dermatitis. Sodium hyaluronate is the key water-regulating substance in human skin. Sodium hyaluronate has high viscoelasticity and lubricity. When sodium hyaluronate solution is applied on the surface of skin, it forms an air permeable layer that keeps skin moist and smooth. Small molecular weight sodium hyaluronate can penetrate into the dermis where it combines with water to promote microcirculation, nutrient absorption, and metabolism. Glycyrrhetinic acid reduces inflammation and is believed to have immunomodulatory properties.

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***Numoisyn® Liquid***

Numoisyn® Liquid is an oral solution used to replace natural saliva when salivary glands are damaged. The viscosity of Numoisyn® Liquid is similar to that of natural saliva. Linseed extract in Numoisyn® Liquid contains mucins that provide superior viscosity and reduced friction compared to water or carboxymethylcellulose or CMC solutions. Linseed extract significantly reduces the symptoms of dry mouth with increasing effect over time while Numoisyn® Liquid is used.

***Numoisyn® Lozenges***

Numoisyn® Lozenges dissolve slowly while moved around in the mouth. They contain sorbitol and malic acid to stimulate normal salivation and provide temporary relief of dry mouth in patients who have some residual secretory function and taste perception. Numoisyn® Lozenges support saliva s natural protection of teeth so that teeth are not damaged with repeated and use of the lozenges. They are sugar free and buffered with calcium to protect teeth. Numoisyn® Lozenges have been demonstrated to be safe and effective for long-term use and are well tolerated by patients. Use of Numoisyn® Lozenges improves subjective symptoms of dry mouth and does not cause bacteria or plaque formation or loss of tooth enamel hardness.

**Business Strategy**

In September 2008, we announced a revision of our operating plan to concentrate our resources on the advancement of our lead drug sapacitabine. Consistent with the revised operating plan, during the second and third quarters of 2009, we further reduced our workforce across all locations by twenty six (26) people making a total reduction of fifty one (51) people, or 63% of our workforce, since September 2008. With these reductions and our cost-containment efforts, we currently anticipate that our cash and cash equivalents of approximately $11.5 million at December 31, 2009 together with the funds raised following the year-end totaling approximately $18.8 million in gross proceeds, are sufficient to meet our anticipated short-term working capital needs and fund our current operations, including on-going sapacitabine clinical trials, for at least the next twelve months. However, we cannot be certain that we will be able to raise sufficient funds to complete the development and commercialize any of our product candidates currently in clinical development, should they succeed.

***Focus on the cell cycle and cancer***

Our core area of expertise is in cell cycle biology and our scientists include recognized leaders in this field. In addition, our senior management has extensive experience in research, preclinical and clinical development and sales and marketing. Thus, we believe that we are well placed to exploit the significant opportunities that this area offers for new drug discovery and development for the following reasons:

- The novel, mechanism-targeted cell cycle drugs we are developing are designed to be highly selective in comparison to conventional chemotherapies, potentially inducing death in cancer cells while sparing most normal cells which may give rise to fewer side-effects.
- We believe that our sapacitabine is the only orally available nucleoside analogue presently being tested in Phase 2 trials in AML and MDS and seliciclib is the only orally available CDK inhibitor currently in Phase 2 trials. We believe that we are well positioned to realize some of the market potential of such drugs.

***Develop anticancer drug candidates in all phases of the cell cycle and multiple compounds for particular cell cycle targets***

Targeting a broad development program focused on multiple phases of the cell cycle allows us to minimize risk while maximizing the potential for success and also to develop products that are complementary to one another.

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***Enter into partnering arrangements selectively, while developing our own sales and marketing capability***

We currently retain virtually all marketing rights to the compounds associated with our current clinical-stage drug programs. To optimize our commercial return, we intend to enter into selected partnering arrangements, and to leverage our sales and marketing capability by retaining co-promotion rights as appropriate. Historically, we have planned to develop compounds through the Phase 2 proof-of-efficacy stage before seeking a partner. We may be prepared to enter into partnering arrangements earlier than Phase 2 proof-of-concept trials in connection with drug programs outside our core competency in oncology.

**Patents, Proprietary Technology and Collaborations**

We consider intellectual property rights to be vital and use a variety of methods to secure, protect and evaluate these rights. These include:

Ownership and enforcement of patent rights;

Patent applications covering our own inventions in fields that we consider important to our business strategy;

License agreements with third parties granting us rights to patents in fields that are important to our business strategy;

Invention assignment agreements with our employees and consultants;

Non-compete agreements with our key employees and consultants;

Confidentiality agreements with our employees, consultants, and others having access to our proprietary information;

Standard policies for the maintenance of laboratory notebooks to establish priority of our inventions;

Freedom to use studies from patent counsel;

Material transfer agreements; and

Trademark protection.

In addition to our 27 United States patents, we own 11 patents that were granted by the European Patent Office, or EPO, for designated European countries, and 27 issued patents in other countries. The European granted patents expire between 2015 and 2022. In addition to the licenses we hold under the 6 patents issued in the United States, we hold licenses under 53 issued patents worldwide, seven granted by the EPO for designated European countries and 46 issued in other countries. The licensed European granted patents expire between 2012 and 2022. Our patent strategy is to file patents on compounds and technologies in countries and jurisdictions that we consider important to our business. We usually file first in the United Kingdom and then extend our applications to other countries through the Patent Cooperation Treaty or PCT. In some cases, we file directly in the United States.

We give priority to obtaining substance of matter claims in the United States, the EPO, Japan and other important markets if such protection is available. We prefer substance of matter claims because they give us rights to the compounds themselves, and not merely a particular use. In addition to substance of matter claims, we seek coverage for solid state forms, polymorphic and crystalline forms, medical uses, combination therapies, pharmaceutical forms of our compounds and synthetic routes where available and appropriate. Claims covering combination therapies and pharmaceutical forms can be valuable because the therapeutic effect of pharmaceuticals used in the anticancer field is often enhanced when individual therapeutics are used in particular combinations. The availability of protection in these areas can, however, vary from jurisdiction to jurisdiction and combination claims are particularly difficult to obtain for many inventions. We own 15 patent applications pending in the United States, 15 before the EPO, four

pending PCT applications still in the international application phase, and over 40 pending patent applications in other countries, including applications first filed within the last twelve months. No assurances can be given that patents will be issued with respect to the pending applications, nor that the claims will provide equivalent coverage in all jurisdictions. In addition to the pending patent applications referred to above that we own, there are 27 pending patent applications worldwide to which we have a license or an option to take a license.

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Our patent filings for the second-generation CDK inhibitor research program exemplify our patent strategy. Out of several series of discovered in this program we have filed patent applications seeking substance of matter protection that may be roughly grouped into 12 patent families. As we have progressed with our research, we have reviewed our patent portfolio and have focused active patent prosecution on 8 patent families covering substance of matter protection. Of these, we have made a European application designating all European Patent Convention member states and direct national filings in the United States, Japan and several additional countries covering the compounds that we believe to be the most promising from a commercial standpoint. The first patent application from this family has resulted in the issuance of two United States patents with substance of matter claims covering a specific genus of compounds showing activity in preclinical and discovery programs. Although issuance of a substance of matter claim in the United States is an indication that other countries may grant similar protection, the pending applications may not result in additional patent protection.

Since publications in the scientific or patent literature often lag behind actual discoveries, we are not certain of being first to make the inventions covered by each of its pending patent applications or the first to file those patent applications. Generally, patent applications in the United States are maintained in secrecy for a period of 18 months or more, which increases the uncertainty we face. Moreover, the patent positions of biotechnology and pharmaceutical companies are highly uncertain and involve complex legal and factual questions. As a result, we cannot predict the breadth of claims allowed in biotechnology and pharmaceutical patents, or their enforceability. To date, there has been no consistent policy regarding the breadth of claims allowed in biotechnology patents. Third parties or competitors may challenge or circumvent our patents or patent applications, if issued. Because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that before we commercialize any of our products, any related patent may expire, or remain in existence for only a short period following commercialization, thus reducing any advantage of the patent and the commercial opportunity of the product.

If patents are issued to others containing valid claims that cover our compounds or their manufacture or use or screening assays related thereto, we may be required to obtain licenses to these patents or to develop or obtain alternative technology. We are aware of several published patent applications, and understand that others may exist, that could support claims that, if granted, would cover various aspects of our developmental programs, including in some cases particular uses of our lead drug candidates, sapacitabine, seliciclib, or other therapeutic candidates, or gene sequences and techniques that we use in the course of our research and development.

In addition, we understand that other applications and patents exist relating to uses of sapacitabine and seliciclib that are not part of our current clinical programs for those compounds. Although we intend to continue to monitor the pending applications, it is not possible to predict whether these claims will ultimately be allowed or if they were allowed what their breadth would be. In addition, we may need to commence litigation to enforce any patents issued to us or to determine the scope and validity of third-party proprietary rights. Litigation would create substantial costs. In one case we have opposed a European patent relating to human aurora kinase and the patent has been finally revoked (no appeal was filed). We are also aware of a corresponding United States patent containing method of treatment claims for specific cancers using aurora kinase modulators which, if held valid, could potentially restrict the use of our aurora kinase inhibitors once clinical trials are completed. If competitors prepare and file patent applications in the United States that claim technology that we also claim, we may have to participate in interference proceedings in the United States Patent and Trademark Office to determine which invention has priority. These proceedings could result in substantial costs, even if the eventual outcome is favorable to us. An adverse outcome in litigation could subject us to significant liabilities to third parties and require us to seek licenses of the disputed rights from third parties or to cease using the technology, even a therapeutic product, if such licenses are unavailable or too expensive.

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**Licenses**

Several of our programs are based on technology licensed from others. Our breach of an existing license or failure to obtain a license to technology required to develop, test and commercialize our products may seriously harm our business.

***Sapacitabine***

We have entered into a license agreement with Daiichi-Sankyo Co., Ltd. of Japan or Daiichi-Sankyo with respect to patents and patent applications covering the sapacitabine compound. Daiichi-Sankyo filed patent applications claiming sapacitabine and certain crystalline forms of sapacitabine and methods for its preparation and use which encompass our chosen commercial development form as well as related know-how and materials. The Daiichi-Sankyo agreement commenced on September 10, 2003. The issued patents for the sapacitabine compound cover the United States, EPO, Japan and 19 other countries. These patents expire between 2012 and 2014. The issued patents for the crystalline forms cover the United States, EPO, Japan and ten other countries, with patents pending in a further four countries. These patents expire in 2022. It may be possible to extend the term of a patent in the United States, Europe or Japan for up to five years to the extent it covers the sapacitabine compound or its crystalline form upon regulatory approval of that compound in the United States, Europe or Japan, but there is no assurance that we will be able to obtain any such extension. The license grants us the exclusive right to exploit and sublicense the sapacitabine compound and any other products covered by the patents and patent applications owned by Daiichi-Sankyo. The license originally was subject to certain third party rights related to certain countries but the license has been extended and is now worldwide. The license agreement also grants us nonexclusive, sublicensed rights to CNDAC, both a precursor compound and initial metabolite of sapacitabine.

We are under an obligation to use reasonable endeavors to develop a product and obtain regulatory approval to sell a product and we have agreed to pay Daiichi-Sankyo an up-front fee, reimbursement for Daiichi-Sankyo s enumerated expenses, milestone payments and royalties on a country-by-country basis. Under this agreement, aggregate milestone payments totaling $11.7 million could be payable subject to achievement of all the specific contractual milestones and our decision to continue with these projects. The up-front fee and certain past reimbursements have been paid. Royalties are payable in each country for the term of patent protection in the country or for ten years following the first commercial sale of licensed products in the country, whichever is later. Royalties are payable on net sales. Net sales are defined as the gross amount invoiced by us or our affiliates or licensees, less discounts, credits, taxes, shipping and bad debt losses. The agreement extends from its commencement date to the date on which no further amounts are owed under it. If we wish to appoint a third party to develop or commercialize a sapacitabine-based product in Japan, within certain limitations, Daiichi-Sankyo must be notified and given a right of first refusal to develop and/or commercialize in Japan. In general, the license may be terminated by us for technical, scientific, efficacy, safety, or commercial reasons on six months notice or twelve if after launch of sapacitabine-based product or by either party for material default. In addition, pursuant to the Daiichi-Sankyo license, we are required to use commercially reasonable efforts to commercialize products based on the licensed rights and to use reasonable efforts to obtain regulatory approval to sell