

CYTRX CORP
Form S-3
December 06, 2012
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As filed with the Securities and Exchange Commission on December 6, 2012

Reg. No. 333-

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM S-3

REGISTRATION STATEMENT

UNDER

THE SECURITIES ACT OF 1933

CYTRX CORPORATION

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

CytRx Corporation

58-1642750
(I.R.S. Employer
Identification No.)

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11726 San Vicente Boulevard, Suite 650

Los Angeles, California 90049

(Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)

Steven A. Kriegsman

President and Chief Executive Officer

CytRx Corporation

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Los Angeles, California 90049

(310) 826-5648

(Name, address, including zip code, and telephone number, including area code, of agent for service)

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Approximate date of commencement of proposed sale to public: From time to time after the effective date of this registration statement.

If the only securities being registered on this form are being offered pursuant to dividend or interest reinvestment plans, please check the following box. "

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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. x

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, 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. (Check one):

| | |
|---|---|
| Large accelerated filer <input type="checkbox"/> .. | Accelerated filer <input type="checkbox"/> p |
| Non-accelerated filer <input type="checkbox"/> .. (Do not check if a smaller reporting company) | Smaller reporting company <input type="checkbox"/> .. |

CALCULATION OF REGISTRATION FEE

| Title of each class of securities to be registered | Proposed maximum aggregate offering price(1) | Amount of registration fee |
|--|--|----------------------------|
| Common Stock, par value \$.001 per share(2) | | |
| Preferred Stock, \$.01 par value per share | | |
| Warrants | | |
| Units | | |
| Total(3) | \$100,000,000(4) | \$13,640 |

- (1) The securities registered by this registration statement may be sold separately, together with other securities registered hereunder or as units consisting of a combination of such securities. Pursuant to Rule 457(o) under the Securities Act of 1933 and General Instruction II.D to Form S-3 under the Securities Act of 1933, the number of shares, warrants or units of each class of securities registered hereunder is not specified. There is being registered hereunder an indeterminate amount of common stock, preferred stock, warrants and units of the registrant as may from time to time be issued at indeterminate prices. The maximum offering price per class of securities will be determined from time to time by the registrant in connection with the issuance of the securities registered by this registration statement. However, in no event will the maximum aggregate offering price of all securities issued under this registration statement exceed \$100,000,000 or such lesser aggregate amount permitted under General Instruction I.B.6 to Form S-3 under the Securities Act of 1933.
- (2) Each share of common stock will be accompanied by one Series A Junior Participating Preferred Stock Purchase Right that trades with the common stock. The value, if any, attributable to this right is reflected in the market price of common stock. Prior to the occurrence of certain events, none of which has occurred as of the date of this registration statement, the rights will not be exercisable or evidenced

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- separately from the common stock.
- (3) Pursuant to Rule 416 under the Securities Act of 1933, this registration statement also registers such indeterminate amounts of securities as may be issued upon conversion of, or in exchange for, the securities registered hereunder and such indeterminate number of shares of common stock and preferred stock as may be issued from time to time upon conversion or exchange as a result of stock splits, stock dividends or similar transactions.
- (4) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(o) under the Securities Act of 1933.

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 OR UNTIL THIS REGISTRATION STATEMENT SHALL BECOME EFFECTIVE ON SUCH DATE AS THE 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. These securities may not be sold until the registration statement filed with the Securities and Exchange Commission becomes effective. This prospectus is not an offer to sell these securities, and it is not a solicitation of an offer to buy these securities, in any state where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DECEMBER 6, 2012

PROSPECTUS

\$100,000,000

We may offer and sell from time to time up to \$100,000,000 in the aggregate of shares of our common stock, shares of our preferred stock and warrants in amounts, at prices and on terms that we will decide at the time of the offering. These securities may be offered and sold separately, together or as units with other securities. Each share of our common stock to be offered and sold is accompanied by one Series A Junior Participating Preferred Stock Purchase Right that trades with our common stock.

We will provide the specific terms of these offers and sales in supplements to this prospectus. This prospectus may not be used to sell securities unless accompanied by a prospectus supplement. You should read this prospectus and the prospectus supplement carefully before you invest. We may offer securities directly to investors or through agents, underwriters or dealers. If any agents, underwriters or dealers are involved in the sale of any of our securities, their names and any applicable purchase prices, fees, commissions or discount arrangements will be set forth in the prospectus supplement.

Our common stock is traded on The Nasdaq Capital Market under the symbol CYTR. On December 5, 2012, the last sale price of our common stock as reported on The NASDAQ Capital Market was \$2.00.

An investment in our securities involves significant risks. Before purchasing any securities, you should consider carefully the risks referred to under Risk Factors on page 7 in this prospectus and in the prospectus supplement.

NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED THESE SECURITIES OR DETERMINED THAT THIS PROSPECTUS IS COMPLETE OR ACCURATE. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

The date of this prospectus is _____, 2012

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement utilizing the shelf registration process that we filed with the Securities and Exchange Commission, or the SEC, to permit us to offer and sell the securities described in this prospectus in one or more transactions. The plan of distribution of the securities is described in this prospectus under the heading Plan of Distribution.

As permitted by the rules and regulations of the SEC, the registration statement filed by us includes additional information not contained in this prospectus. You may read the registration statement and the other reports we file with the SEC at the SEC's web site or at the SEC's offices described below under the heading Where You Can Find Additional Information.

This prospectus provides you with a general description of the securities we may offer. Each time securities are sold, we will provide a prospectus supplement that will contain specific information about the terms of that offering. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and the prospectus supplement, together with additional information described in this prospectus under the heading Where You Can Find More Information.

You should rely only on the information provided in this prospectus and in the prospectus supplement, including any information incorporated by reference. For more details on information incorporated herein by reference, you should review the discussion contained under the heading Incorporation of Certain Documents by Reference. We have not authorized anyone to provide you with information different from that contained or incorporated by reference in this prospectus and in the prospectus supplement. We are offering the securities only in jurisdictions where offers are permitted. You should not assume that the information in this prospectus or the prospectus supplement is accurate at any date other than the date indicated on the cover page of these documents.

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In this prospectus, we sometimes refer to CytRx Corporation as CytRx, to our former subsidiary, RXi Pharmaceuticals Corporation, as RXi, and to Innovive Pharmaceuticals, Inc., which we acquired in September 2008 and merged into CytRx in December 2008, as Innovive. References in this prospectus and the prospectus supplement to we, us, our or the company refer to CytRx, alone, unless otherwise indicated.

NOTE ON FORWARD-LOOKING STATEMENTS

Some of the statements contained or incorporated by reference in this prospectus or in the prospectus supplement may include forward-looking statements that reflect our current views with respect to our research and development activities, business strategy, business plan, financial performance and other future events. These statements include forward-looking statements both with respect to us, specifically, and the biotechnology sector, in general. We make these statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Statements that include the words expect, intend, plan, believe, project, estimate, may, should, anticipate, will and statements of a future or forward-looking nature identify forward-looking statements for purposes of the federal securities laws or otherwise.

All forward-looking statements involve inherent risks and uncertainties, and there are or will be important factors that could cause actual results to differ materially from those indicated in these statements. We believe that these factors include, but are not limited to, those factors set forth under the caption Risk Factors in this prospectus and in any prospectus supplement and under the captions Business, Legal Proceedings, Management's Discussion and Analysis of Financial Condition and Results of Operations, Quantitative and Qualitative Disclosures About Market Risk and Controls and Procedures in our most recent Annual Report on Form 10-K and our most recent Quarterly Report on Form 10-Q, all of which you should review carefully. Please consider our forward-looking statements in light of those risks as you read this prospectus and the prospectus supplement. We undertake no obligation to publicly update or review any forward-looking statement, whether as a result of new information, future developments or otherwise.

If one or more of these or other risks or uncertainties materializes, or if our underlying assumptions prove to be incorrect, actual results may vary materially from what we anticipate. All subsequent written and oral forward-looking statements attributable to us or individuals acting on our behalf are expressly qualified in their entirety by this Note. Before purchasing any securities, you should consider carefully all of the factors set forth or referred to in this prospectus and in the prospectus supplement that could cause actual results to differ.

Table of Contents**ABOUT CYTRX****Overview**

We are a biopharmaceutical research and development company specializing in oncology. Our oncology pipeline includes two programs in clinical development for cancer indications: aldoxorubicin (formerly known as INNO-206) and tamibarotene. With our tumor-targeted doxorubicin conjugate aldoxorubicin, we have initiated an international Phase 2b clinical trial as a treatment for soft tissue sarcomas, completed a Phase 1b/2 clinical trial primarily in the same indication and recently initiated a Phase 1b pharmacokinetics clinical trial in patients with metastatic solid tumors, a Phase 2 trial for patients with advanced pancreatic ductal adenocarcinomas and a Phase 1b study of aldoxorubicin in combination with doxorubicin in patients with advanced solid tumors. We held a positive meeting with the Food and Drug Administration (FDA) to discuss a potential Phase 3 pivotal trial as a therapy for patients with soft tissue sarcomas whose tumors have progressed following treatment with chemotherapy, and are planning to submit a special protocol assessment with respect to that potential trial. Tamibarotene is being tested in a double-blind, placebo-controlled, international Phase 2b clinical trial in patients with non-small-cell lung cancer, and is in a Phase 2 clinical trial as a treatment for acute promyelocytic leukemia (APL). We completed our evaluation of a third drug candidate, bafetinib, in the ENABLE Phase 2 clinical trial in high-risk B-cell chronic lymphocytic leukemia (B-CLL), and plan to seek a partner for further development of bafetinib.

Our Product Candidate Pipeline

The following table summarizes our product candidates and their current or impending stages of development:

| Technology | Product candidate | Indication(s) | Stage of development |
|---------------------------|--------------------------|--|-----------------------------|
| Doxorubicin conjugate | Aldoxorubicin | Soft tissue sarcomas | Phase 2b |
| | | In combination with doxorubicin in patients with advanced solid tumors | Phase 1b |
| | | Advanced pancreatic ductal adenocarcinomas | Phase 2 |
| Synthetic retinoid | Tamibarotene | NSCLC (non-small-cell lung cancer) | Phase 2b |
| | | APL (acute promyelocytic leukemia) | Phase 2b |
| Tyrosine kinase inhibitor | Bafetinib | B-CLL (B-cell chronic lymphocytic leukemia) | Phase 2 complete |

Our Clinical Development Programs

Our current clinical development programs are discussed below.

Aldoxorubicin

Aldoxorubicin (formerly INNO-206) is a tumor-targeted conjugate of the commonly prescribed chemotherapeutic agent doxorubicin. Specifically, it is the (6-Maleimidocaproyl) hydrazone of doxorubicin. Essentially, this chemical is doxorubicin (DOXO) attached to an acid sensitive linker known as EMCH.

Aldoxorubicin for the Treatment of Cancer. Anthracyclines are a class of drugs that are among the most commonly used agents in the treatment of cancer. Doxorubicin, the first anthracycline to gain FDA approval, has demonstrated efficacy in a wide variety of cancers including breast cancer, lung cancer, sarcomas, and lymphomas. However, due to the uptake of doxorubicin by various parts of the body, it is associated with side effects such as cumulative cardiotoxicity, myelosuppression (decreased production of blood cells by bone marrow), gastrointestinal disorders, mucositis (inflammation of the mucous membranes lining the digestive tract, including the mouth), stomatitis (inflammation of the mouth's soft tissue), and extravasation (the leakage of intravenous drugs from the vein into the surrounding tissue).

We believe aldoxorubicin has attributes that may improve on native doxorubicin, including the potential to reduce adverse events and improve efficacy and the ability to target the tumor more accurately than native doxorubicin.

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Our anticipated mechanism of action for aldoxorubicin is as follows:

after administration, aldoxorubicin rapidly binds circulating albumin through the EMCH linker;

circulating albumin preferentially accumulates in tumors, bypassing concentration in other non-tumor sites, including the heart, liver and the gastrointestinal tract;

once albumin-bound aldoxorubicin reaches the tumor, the acidic environment of the tumor causes cleavage of the acid sensitive linker; and

free doxorubicin is released at the site of the tumor and is taken up by the cancer cells.

Pre-clinical data. In a variety of preclinical models, aldoxorubicin was superior to doxorubicin at equitoxic doses in its ability to allow an increase in the total doxorubicin dose, its antitumor efficacy, and its safety, including a reduction in cardiotoxicity. Animal studies conducted by aldoxorubicin inventor Dr. Felix Kratz, Department of Medical Oncology, Clinical Research, at the Tumor Biology Center in Freiburg, Germany, demonstrated statistically significant efficacy compared to either placebo or native doxorubicin against breast, ovarian, pancreatic and small cell lung cancers growing in immunodeficient mice.

Clinical data. A Phase 1 study of aldoxorubicin that demonstrated safety and objective clinical responses in several tumor types was completed in 2005 and presented at the March 2006 Krebskongress meeting in Berlin. In this study, doses were administered every three weeks at up to six times the standard dose of doxorubicin without an increase in side effects over those historically observed with native doxorubicin. Twenty-three of 35 evaluable patients had either an objective clinical (partial) response or stable disease. Objective clinical responses were observed in patients with sarcoma, breast, and small cell lung cancers.

We completed a Phase 1b/2 clinical trial with aldoxorubicin in patients with advanced solid tumors and presented favorable data at the American Society for Clinical Oncology Meeting in June, 2012. In that Phase 1b/2 clinical trial, clinical benefit (defined as partial response or stable disease of more than four months following up to eight cycles of treatment) with aldoxorubicin at the maximum tolerated dose was shown in 10 of 13 (76.9%) evaluable patients with relapsed or refractory soft tissue sarcoma.

In addition, best response for the 13 evaluable soft tissue sarcoma trial subjects included the following: five (38.5%) achieved partial response, as defined as tumor shrinkage of more than 30%; seven (53.8%) showed prolonged stable disease (defined as tumor shrinkage <30% from baseline or tumor growth <20% from the nadir); eight (61.5%) had tumor shrinkage; and five of eight patients (62.5%) who demonstrated either partial responses or prolonged stable disease after treatment with aldoxorubicin had been previously treated with doxorubicin and had failed to respond. There were no observed cardiac toxicities and no drug-related patient deaths. The most common adverse event, neutropenia, also observed with doxorubicin treatment, resolved prior to the start of the next treatment. Median estimated progression-free survival for advanced soft tissue sarcoma patients in the trial was 6.4 months with a range of 1.0 to more than 10.7 months.

Development Plan. In December 2011, we initiated our international Phase 2b clinical trial to evaluate the preliminary efficacy and safety of aldoxorubicin as a first-line therapy in patients with advanced soft tissue sarcoma who are ineligible for surgery. The Phase 2b clinical trial will provide the first direct clinical trial comparison of aldoxorubicin with native doxorubicin, the only approved chemotherapy agent for the treatment of soft tissue sarcomas, which is dose-limited due to toxicity, as a first-line therapy.

The Phase 2b clinical trial with aldoxorubicin in patients with soft tissue sarcomas is an international trial under the direction of world-renowned expert in soft tissue sarcoma treatment Sant P. Chawla, M.D., F.R.A.C.P., Director of the Sarcoma Oncology Center in Santa Monica, California. Dr. Chawla also is acting as principal investigator for our ongoing Phase 1b/2 clinical trial with aldoxorubicin.

The Phase 2b clinical trial's primary objectives are to measure the progression-free survival, tumor response and overall survival of patients with advanced soft tissue sarcomas treated with aldoxorubicin. This clinical trial also will assess the safety of aldoxorubicin compared to doxorubicin in this patient population through a number of indicators, including the frequency and severity of adverse events. The open-label trial will enroll 105 patients with metastatic, locally advanced or unresectable soft tissue sarcoma at approximately 30 study centers in the United States, Hungary, Romania, Ukraine, Russia, India and Australia.

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In addition, we have initiated a Phase 1b pharmacokinetics clinical trial in patients with metastatic solid tumors, a Phase 2 trial for patients with advanced pancreatic ductal adenocarcinomas and a Phase 1b study of aldoxorubicin in combination with doxorubicin in patients with advanced solid tumors.

We recently held a positive meeting with the Food and Drug Administration (FDA) to discuss a potential Phase 3 pivotal trial as a therapy for patients with soft tissue sarcomas whose tumors have progressed following treatment with chemotherapy, and plan to submit a special protocol assessment with respect to that potential trial.

Tamibarotene

Tamibarotene is an orally available, synthetic retinoid rationally designed to overcome resistance and reduce the toxic side effects of differentiation therapy with all-trans retinoic acid, or ATRA, a component of the current first-line treatment for APL.

Tamibarotene for the treatment of NSCLC. More than 220,000 new cases of lung cancer occur in the United States each year, and more than 1.5 million occur annually worldwide. Deaths due to lung cancer account for the majority of cancer-related deaths and the five-year survival ranges between 8% and 15%. Non-small cell-lung cancer, or NSCLC, accounts for approximately 85% of all lung cancers, with the subsets adenocarcinoma representing 35% to 40%, squamous cell carcinoma accounting for 25% to 30% and large cell carcinoma accounting for 10% to 15%.

A Phase 2 clinical trial of 107 patients conducted by Arrieta *et al.* and published in the peer-reviewed Journal of Clinical Oncology (2010; 28: 3463-3471) compared ATRA added to a regimen of paclitaxel plus cisplatin to a regimen of paclitaxel plus cisplatin alone as a treatment for patients with advanced NSCLC. The group administered ATRA plus the chemotherapy agents showed improved response rates of 55.8% versus 25.4%, and increased progression-free survival of 8.9 months versus 6.0 months. Median overall survival was increased from 9.5 months to 23.5 months when ATRA was added to the above chemotherapy regimen, representing a 14-month median extension of life.

Tamibarotene was developed to overcome resistance to ATRA. In vitro, tamibarotene is approximately ten times more potent than ATRA, and tamibarotene has a lower affinity for cellular retinoic acid binding protein, or CRABP, which we believe should allow increased cellular exposure after administration. This may enhance tamibarotene's potential efficacy, because patients may be able to experience benefits from the drug for a more prolonged period. Tamibarotene does not bind the RAR- α receptor, the major retinoic acid receptor in the dermal epithelium, which should lessen the occurrence of skin toxicities.

Development Plan. We have initiated an international, randomized Phase 2b clinical trial, in which patients with stage IIIB (with pleural effusions, or fluid in the chest cavity) or stage IV NSCLC will be treated with up to six cycles of paclitaxel plus carboplatin and either tamibarotene or placebo. The primary objective of the clinical trial is to determine the objective response rate (complete and partial responses) and progression-free survival. Secondly, the study will evaluate overall survival, quality-of-life and the pharmacokinetics of tamibarotene in this population. The clinical trial, which is expected to enroll approximately 140 patients, is being conducted in several clinical sites in the United States, Mexico, Eastern Europe and India.

Tamibarotene for the treatment of APL. Acute promyelocytic leukemia, or APL, is a specific type of acute myeloid leukemia characterized by the t(15;17) translocation, which fuses the promyelocytic leukemia, or PML, gene on chromosome 15 to the retinoic acid receptor, or RAR α , gene on chromosome 17. This fusion causes abnormal cell growth.

Differentiation therapy with ATRA is the basis for the treatment of APL. Differentiation therapy causes leukemic promyelocytes to mature and undergo cell death. Patients typically receive ATRA in combination with chemotherapy as the initial therapy, followed by anthracycline-based consolidation therapy designed to produce complete remission. The majority of patients treated this way experience a complete remission of disease. Current

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National Comprehensive Cancer Network guidelines recommend that patients then undergo one to two years of maintenance therapy with ATRA to prevent a recurrence. ATRA therapy is associated with several toxicities, the most serious of which is retinoic acid syndrome, or RAS. RAS, which occurs in up to 25% of patients treated with ATRA, is a serious and potentially fatal complication characterized by fever, dyspnea (breathing difficulties), weight gain, pulmonary infiltrates (abnormal accumulation in the lungs), and pleural or pericardial effusions (excess fluid around the lungs or heart).

Patients that initially respond to front-line therapy with ATRA plus chemotherapy sometimes relapse, and some of these patients fail to respond to a second course of treatment with ATRA. Currently, patients who fail ATRA-based therapy are treated with arsenic trioxide, a compound administered intravenously and associated with significant toxicity, including irregular heartbeat. There currently is no standard of care for patients who do not respond to ATRA and arsenic trioxide, or who respond but subsequently relapse. In 2007, the FDA granted Orphan Drug Designation and Fast Track Designation for the use of tamibarotene in patients with APL who relapse after treatment with ATRA and chemotherapy, then ATRA plus arsenic trioxide.

Pre-clinical data. In preclinical models, tamibarotene was superior to ATRA in its ability to cause APL cells to differentiate and die. In the clinical setting, in vitro response to tamibarotene appeared predictive of clinical response, including activity in patients who had a poor response to ATRA.

Clinical data. Tamibarotene is approved in Japan under the brand name Amnolake for use in relapsed or refractory APL. The approval was based on data from two studies in Japanese patients. In the pivotal study, the effectiveness of orally administered tamibarotene was administered to 42 patients with APL, 39 of whom were evaluable for response. Patients included individuals who had never received treatment for APL and patients who had been previously treated with ATRA. Tamibarotene was administered orally at a dose of 6 mg/m²/day for eight weeks. The overall complete response rate in these patients was 61.5%. In patients who had a recurrence of APL following ATRA therapy, the response rate was 81%. RAS was reported in three patients, or 7.3% of the patient group.

Development Plan. Although there is currently a Special Protocol Assessment (SPA) in place with the FDA for a Phase 2 registration clinical trial, known as STAR-1, to evaluate the efficacy and safety of tamibarotene as a third-line treatment for APL, there are currently no open sites and we are not enrolling patients in the trial. We have reported that, of the 11 patients previously enrolled in the STAR-1 trial, three (27%) achieved a hematologic complete response and four (36%) a morphologic leukemia-free state, and that a patient with a rare form of APL called sarcomatous acute promyelocytic leukemia, or chloromas, had a complete response to treatment with tamibarotene which has been ongoing for more than two years.

Bafetinib

Bafetinib (formerly INNO-406) is an orally bioavailable, rationally designed inhibitor of several Src kinases developed by the Japanese pharmaceutical company Nippon Shinyaku to overcome some of the limitations of Gleevec and other tyrosine kinase inhibitors in resistant chronic myelogenous leukemia, or CML. In addition to its Bcr-Abl inhibitory properties, bafetinib is a potent and specific inhibitor of Lyn and Fyn kinases. These kinases are reported to be involved in both solid and hematological cancers. Lyn kinase s involvement in the B-cell signaling pathway led us to evaluate bafetinib in B-cell malignancies such as chronic lymphocytic leukemia (CLL). We hold rights to bafetinib in all territories except Japan.

Phase I Study. In November 2008, we announced that bafetinib demonstrated clinical responses in patients with CML in a Phase 1 clinical trial conducted in patients with CML and other leukemias that have a certain mutation called the Philadelphia Chromosome (Ph+) and are intolerant of or resistant to Gleevec and, in some cases, second-line tyrosine kinase inhibitors such as dasatinib (Sprycel[®]) and nilotinib (Tasigna[®]). The clinical trial was designed to identify the optimal dose for possible future studies by escalating doses from 30 mg once per day to up to 480 mg twice per day in a total of 56 patients with Ph+ leukemias. Of the patients, 31 had CML in chronic phase (CML-CP), nine were in accelerated phase (CML-AP), seven were in blast phase (CML-BP), and nine had Ph+ acute lymphocytic leukemia. The clinical trial was conducted at seven clinical sites in the United States, Germany, and Israel, with Hagop Kantarjian, M.D., Professor & Chairman, Department of Leukemia, The University of Texas, M.D. Anderson Cancer Center, serving as the Principal Investigator. In the 31 patients with CMP-CP, a major cytogenetic response rate of 19.4% was seen.

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The maximum tolerated dose was determined to be 240-360 mg given twice per day, based on evidence of increasing potential liver toxicity at higher doses. Common adverse events (observed in greater than 20% of patients in the 240 mg twice per day dose group) were gastrointestinal toxicity, swelling, and fatigue. There was no evidence of fluid accumulating around the lungs, or significant changes in a certain heart rhythm called QTc prolongation, which are serious side effects known to occur in patients treated with approved drugs for this indication. Approximately 13% of patients across all dose groups discontinued dosing due to unacceptable toxicity.

Bafetinib for B-CLL. B-cell chronic lymphocytic leukemia, or B-CLL, is the most common form of leukemia in adults in Western countries. More than 16,000 new cases of B-CLL are reported in the United States alone each year; however, up to an estimated 40% of cases may not be reported due to under-diagnosis and lack of placement in cancer registries. Virtually all patients are older than 55 years at presentation, with an average age of 70 years. Patients in the high-risk B-CLL classification have a median overall survival period of one to five years.

Our Phase 2 proof-of-concept clinical trial to evaluate the preliminary efficacy and safety of its oncology drug candidate bafetinib in patients with high-risk B-cell chronic lymphocytic leukemia (B-CLL) was initiated in May 2010. In that clinical trial, high-risk B-CLL patients who had failed treatment with first-line agents were self-administered oral doses of bafetinib twice daily. We have announced that results from that clinical trial demonstrated bafetinib's clinical activity and preliminary safety in patients with relapsed or refractory B-CLL.

We plan to seek a partner for any further development of bafetinib.

Corporate Information

We are a Delaware corporation, incorporated in 1985. Our corporate offices are located at 11726 San Vicente Boulevard, Suite 650, Los Angeles, California 90049, and our telephone number is (310) 826-5648. Our web site is located on the worldwide web at <http://www.cytrx.com>. We do not incorporate by reference into this prospectus the information on, or accessible through, our website, and you should not consider it as part of this prospectus.

RISK FACTORS

You should carefully consider the risks described below before making an investment decision. The risks described below are not the only ones we face. Additional risks we are not presently aware of or that we currently believe are immaterial may also impair our business operations. Our business could be harmed by any of these risks. The trading price of our common stock could decline due to any of these risks, and you may lose all or part of your investment. In assessing these risks, you should also refer to the other information contained or incorporated by reference in this prospectus, including our financial statements and related notes. We have attempted to identify below the major factors that could cause differences between actual and planned or expected results, but we cannot assure you that we have identified all such factors.

Risks Associated With Our Business and Industry

We have operated at a loss and will likely continue to operate at a loss for the foreseeable future.

We have operated at a loss due to our ongoing expenditures for research and development of our product candidates and for general and administrative purposes and lack of significant recurring revenue. We incurred a net loss of \$14.4 million for the year ended December 31, 2011, a net profit of \$0.4 million attributable to a gain from the sale of RXi shares and other marketable securities for the year ended December 31, 2010, a net loss of \$4.8 million, including a gain from the sale of RXi shares, for the year ended December 31, 2009, and a net loss of \$21.8 million for the nine months ended September 30, 2012. We had an accumulated deficit as of September 30, 2012 of \$232.8 million. We are likely to continue to incur losses unless and until we are able to commercialize one or more of our product candidates. These losses, among other things, have had and will continue to have an adverse effect on our stockholders' equity and working capital. Because of the numerous risks and uncertainties associated with our product development efforts, we are unable to predict when we may become profitable, if at all. If we do not become profitable or are unable to maintain future profitability, the market value of our common stock will be adversely affected.

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Because we have no source of significant recurring revenue, we must depend on financing to sustain our operations.

Developing products and conducting clinical trials require substantial amounts of capital. To date, we have relied primarily upon proceeds from sales of our equity securities, sales of our shares of common stock of our former RXi subsidiary, and the exercise of options and warrants to generate funds needed to finance our business and operations. We will need to raise additional capital to, among other things:

fund our clinical trials and pursue regulatory approval of our existing and possible future product candidates;

expand our research and development activities;

finance our general and administrative expenses;

acquire or license new technologies;

prepare, file, prosecute, maintain, enforce and defend our patent and other proprietary rights; and

develop and implement sales, marketing and distribution capabilities to successfully commercialize any product for which we obtain marketing approval and choose to market ourselves.

Our revenues were \$0.3 million, \$0.1 million and \$9.5 million, respectively, for the years ended December 31, 2011, 2010 and 2009, and we had no revenue in the nine months ended September 30, 2012. Our revenues in 2009 included \$9.4 million of deferred revenue recognized from our sale in August 2006 of a one-percent royalty interest in worldwide sales of arimoclomol for the treatment of ALS to the privately funded ALS Charitable Remainder Trust, or ALSCRT. Pursuant to an amendment signed between us and the beneficiary of the ALSCRT on August 6, 2009, we were released from all restrictions on the use of any proceeds previously paid to us in connection with the arrangement. As a result, we recognized \$6.7 million as service revenue in the third quarter of 2009, which represented the remaining deferred revenue and previously unrecognized portion of the value received. We will have no significant recurring revenue unless we are able to commercialize one or more of our product candidates in development, which may require us to first enter into license or other strategic arrangements with third parties.

At September 30, 2012, we had cash and cash equivalents of approximately \$12.5 million and short-term investments of approximately \$10.0 million. On October 23, 2012, we completed an underwritten public offering of 9,200,000 shares of our common stock at a price of \$2.50 per share, resulting in net proceeds to us of approximately \$21.4 million. Management believes that our current resources along with the net proceeds of our recent offering will be sufficient to fund our operations for the foreseeable future. The belief is based in part upon our currently estimated expenditures for the remainder of 2012 and the first nine months of 2013 of approximately \$20.0 million, which includes approximately \$7.8 million for its clinical programs for aldoxorubicin, approximately \$3.0 million for its clinical program for tamibarotene, approximately \$0.2 million for its clinical programs for bafetinib, approximately \$2.1 million for general operation of its clinical programs, and approximately \$6.9 million for other general and administrative expenses. These estimated expenditures are based upon numerous assumptions and subject to many uncertainties, and our actual expenditures may be significantly different.

If we obtain marketing approval and successfully commercialize our product candidates, we anticipate it will take a minimum of several years, and likely longer, for us to generate significant recurring revenue, and we will be dependent on future financing until such time, if ever, as we can generate significant recurring revenue. Our ability to raise capital may be adversely affected by the continued weak economic recovery in the United States. We have no commitments from third parties to provide us with any additional financing, and we may not be able to obtain future financing on favorable terms, or at all. Failure to obtain adequate financing would adversely affect our ability to operate as a going concern. If we raise additional funds by issuing equity securities, dilution to stockholders may result and new investors could have rights superior to holders of the shares issued in this offering. In addition, debt financing, if available, may include restrictive covenants. If adequate funds are not available to us, we may have to liquidate some or all of our assets or to delay or reduce the scope of or eliminate some portion or all of our development programs or clinical trials. We also may have to license to other companies our product candidates or technologies that we would prefer to develop and commercialize ourselves.

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If we do not achieve our development goals in the time frames we estimate, the commercialization of our products may be delayed and our business prospects may suffer. Our estimated expenditures also may prove to be materially inaccurate.

From time to time, we estimate the timing of the accomplishment of various scientific, clinical, regulatory and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of scientific studies and clinical trials and the submission of regulatory filings such as the discussion in this prospectus supplement of the expected timing of certain milestones relating to our aldoxorubicin, tamibarotene and bafetinib clinical development programs.

We also may disclose estimated expenditures or other forecasts for future periods such as the statements above in this prospectus supplement regarding our current estimated expenditures for fiscal year 2012. These and other financial estimates are based on management's current expectations and do not contain any margin of error or cushion for any specific uncertainties, or for the uncertainties inherent in all financial estimates.

The actual timing of milestones and actual expenditures or other financial results can vary dramatically compared to our estimates, in some cases for reasons beyond our control. If we do not meet milestones or financial projections as announced from time to time, the development and commercialization of our products may be delayed and our business prospects may suffer. Our assumptions underlying these estimates may significantly change or prove to be inaccurate. Accordingly, you should not unduly rely on any of these financial estimates.

If our products are not successfully developed and approved by the FDA or foreign regulatory authorities, we may be forced to reduce or curtail our operations.

All of our product candidates in development must be approved by the FDA or corresponding foreign governmental agencies before they can be marketed. The process for obtaining FDA and foreign government approvals is both time-consuming and costly, with no certainty of a successful outcome. This process typically includes the conduct of extensive pre-clinical and clinical testing, including post-approval testing, which may take longer or cost more than we or our licensees, if any, anticipate, and may prove unsuccessful due to numerous factors. Product candidates that may appear to be promising at early stages of development may not successfully reach the market for a number of reasons. The results of preclinical and initial clinical testing of these product candidates may not necessarily be predictive of the results that will be obtained from later or more extensive testing. Companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in advanced clinical trials, even after obtaining promising results in earlier trials.

Numerous factors could affect the timing, cost or outcome of our product development efforts, including the following:

difficulty in enrolling patients in conformity with required protocols or projected timelines;

requirements for clinical trial design imposed by the FDA;

unexpected adverse reactions by patients in trials;

difficulty in obtaining clinical supplies of the product;

changes in or our inability to comply with FDA or foreign governmental product testing, manufacturing or marketing requirements;

regulatory inspections of clinical trials or manufacturing facilities, which may, among other things, require us or our manufacturers or licensees to undertake corrective action or suspend or terminate the affected clinical trials if investigators find them not to be in compliance with applicable regulatory requirements;

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inability to generate statistically significant data confirming the safety and efficacy of the product being tested;

modification of the product during testing; and

reallocation of our limited financial and other resources to other clinical programs.

It is possible that none of the product candidates we develop will obtain the regulatory approvals necessary for us to begin selling them. The time required to obtain FDA and foreign governmental approvals is unpredictable, but often can take years following the commencement of clinical trials, depending upon the complexity of the product candidate. Any analysis we perform on data from clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent regulatory approval.

Furthermore, even if we obtain regulatory approvals, our products and the manufacturing facilities used to produce them will be subject to continual review, including periodic inspections and possible mandatory post-approval clinical trials by the FDA and other U.S. and foreign regulatory authorities. Any delay or failure in obtaining required approvals or to comply with post-approval regulatory requirements could have a material adverse effect on our ability to generate revenue from the particular product candidate. The failure to comply with any post-approval regulatory requirements also could result in the rescission of the related regulatory approvals or the suspension of sales of the offending product.

Our current and planned clinical trials of our product candidates may fail to show that these product candidates are clinically safe and effective, or that they are better than alternative treatments.

Aldoxorubicin was no more toxic than free doxorubicin in a Phase 1 clinical trial and showed limited biological responses against certain tumors. However, these results may not be reproducible in larger clinical trials, including the ongoing Phase 1b/2 and Phase 2b clinical trials of aldoxorubicin as a treatment for soft tissue sarcomas.

Tamibarotene has been shown to be safe, well-tolerated, and efficacious in the Japanese APL population. However, it is possible that the response to the drug may be different in American or European populations. Furthermore, the efficacy studies that led to approval in Japan occurred prior to the advent of the use of arsenic trioxide, or ATO, for second-line therapy. It is possible that the current use of ATO could alter the safety or efficacy of tamibarotene. The FDA might not accept the Japanese studies as a database for safety. The majority of patients treated with ATRA as a first-line therapy generally experience a complete remission of disease. As a result of the limited population of patients requiring third-line treatment for APL, there is no assurance that we will be successful in recruiting a sufficient number of patients into our ongoing clinical trial of tamibarotene as a third-line treatment for APL in order to demonstrate efficacy. Any FDA-required changes to our clinical development strategy could delay or increase the cost of the trial, adversely affect our ability to demonstrate the efficacy of tamibarotene in the trial or cause us not to pursue clinical development of tamibarotene for one or more of these considerations. Tamibarotene has never been tested in human clinical trials in patients with NSCLC, and there are no assurances that it will be effective in that indication.

Bafetinib demonstrated clinical responses in patients with CML in a Phase 1 clinical trial conducted in patients with CML and other leukemias that have a certain mutation called the Philadelphia Chromosome (Ph+) and are intolerant of or resistant to Gleevec and, in some cases, second-line tyrosine kinase inhibitors. Bafetinib was tested in a human clinical trial in patients with high-risk B-CLL. Of the evaluable patients, approximately 50% had shrinkage of their lymph nodes and/or spleen, which is one of the goals of treatment. Larger trials to determine the efficacy and safety of bafetinib will be required, and there are no assurances that it will be effective in that indication.

Even if our current trials are successful, subsequent trials may not yield statistically significant data indicating that these product candidates are clinically effective. Accordingly, we, or any development partners, may ultimately be unable to provide the FDA with satisfactory data on clinical safety and efficacy sufficient to obtain FDA approval of aldoxorubicin, tamibarotene or bafetinib for any indications.

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We will rely upon third parties for the manufacture of our clinical product supplies.

We do not have the facilities or expertise to manufacture supplies of any of our product candidates. Accordingly, we are dependent upon third-party manufacturers, or potential future strategic alliance partners, to manufacture these supplies. We have manufacturing supply arrangements in place with respect to a portion of the clinical supplies needed for the clinical development programs for aldoxorubicin, tamibarotene and bafetinib. However, we have no supply arrangements for the commercial manufacture of these product candidates or any manufacturing supply arrangements for any other potential product candidates, and we may not be able to secure needed supply arrangements on attractive terms, or at all. Our failure to secure these arrangements as needed could have a materially adverse effect on our ability to complete the development of our products or to commercialize them.

If our product candidates cannot be manufactured in suitable quantities and in accordance with regulatory standards, our clinical trials, regulatory approvals and marketing efforts for such products may be delayed. Such delays could adversely affect our competitive position and our chances of generating significant recurring revenues. If our products cannot be manufactured at an acceptable cost, the commercial success of our products may be adversely affected.

We may rely upon third parties in connection with the commercialization of our products.

The completion of the development of aldoxorubicin, tamibarotene and bafetinib, as well as the marketing of these products, may require us to enter into strategic alliances, license agreements or other collaborative arrangements with other pharmaceutical companies under which those companies will be responsible for one or more aspects of the commercial development and eventual marketing of our products.

Our products may not have sufficient potential commercial value to enable us to secure strategic arrangements with suitable companies on attractive terms, or at all. If we are unable to enter into such arrangements, we may not have the financial or other resources to complete the development of any of our products and may have to sell our rights in them to a third party or abandon their development altogether.

To the extent we enter into collaborative arrangements, we will be dependent upon the timeliness and effectiveness of the development and marketing efforts of our contractual partners. If these companies do not allocate sufficient personnel and resources to these efforts or encounter difficulties in complying with applicable FDA and other regulatory requirements, we may not obtain regulatory approvals as planned, if at all, and the timing of receipt or the amount of revenue from these arrangements may be materially and adversely affected. By entering into these arrangements rather than completing the development and then marketing these products on our own, the profitability to us of these products may decline.

We may be unable to protect our intellectual property rights, which could adversely affect our ability to compete effectively.

We believe that obtaining and maintaining patent and other intellectual property rights for our technologies and potential products is critical to establishing and maintaining the value of our assets and our business. We will be able to protect our technologies from unauthorized use by third parties only to the extent that we have rights to valid and enforceable patents or other proprietary rights that cover them. Although we have rights to patents and patent applications directed to aldoxorubicin, tamibarotene and bafetinib, these patents and applications may not prevent third parties from developing or commercializing similar or identical technologies. In addition, our patents may be held to be invalid if challenged by third parties, and our patent applications may not result in the issuance of patents.

The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in biotechnology patents has emerged to date in the United States and in many foreign countries. The application and enforcement of patent laws and regulations in foreign countries is even more uncertain. Accordingly, we may not be able to effectively file, protect or defend our proprietary rights on a consistent basis. Many of the patents and patent applications on which we rely were issued or filed by third parties prior to the time we acquired rights to them. The validity, enforceability and ownership of those patents and patent applications may be challenged, and if a court decides that our patents are not valid, we will not have the right to stop others from using our inventions. There is also the risk that, even if the validity of our patents is upheld, a court may refuse to stop others on the ground that their activities do not infringe our patents.

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Any litigation brought by us to protect our intellectual property rights could be costly and have a material adverse effect on our operating results or financial condition, make it more difficult for us to enter into strategic alliances with third parties to develop our products, or discourage our existing licensees from continuing their development work on our potential products. If our patent coverage is insufficient to prevent third parties from developing or commercializing similar or identical technologies, the value of our assets is likely to be materially and adversely affected.

We also rely on certain proprietary trade secrets and know-how, especially where we believe patent protection is not appropriate or obtainable. However, trade secrets and know-how are difficult to protect. Although we have taken measures to protect our unpatented trade secrets and know-how, including the use of confidentiality and invention assignment agreements with our employees, consultants and some of our contractors, it is possible that these persons may disclose our trade secrets or know-how or that our competitors may independently develop or otherwise discover our trade secrets and know-how.

If our product candidates infringe the rights of others, we could be subject to expensive litigation or be required to obtain licenses from others to develop or market them.

Our competitors or others may have patent rights that they choose to assert against us or our licensees, suppliers, customers or potential collaborators. Moreover, we may not know about patents or patent applications that our products would infringe. For example, because patent applications do not publish for at least 18 months, if at all, and can take many years to issue, there may be currently pending applications, unknown to us, that may later result in issued patents that our product candidates would infringe. In addition, if third parties file patent applications or obtain patents claiming technology also claimed by us or our licensors in issued patents or pending applications, we may have to participate in interference proceedings in the U.S. Patent and Trademark Office to determine priority of invention. If third parties file oppositions in foreign countries, we may also have to participate in opposition proceedings in foreign tribunals to defend the patentability of our foreign patent applications.

If a third party claims that we infringe its proprietary rights, any of the following may occur:

we may become involved in time-consuming and expensive litigation, even if the claim is without merit;

we may become liable for substantial damages for past infringement if a court decides that our technology infringes a competitor's patent;

a court may prohibit us from selling or licensing our product without a license from the patent holder, which may not be available on commercially acceptable terms, if at all, or which may require us to pay substantial royalties or grant cross licenses to our patents; and

we may have to redesign our product candidates or technology so that it does not infringe patent rights of others, which may not be possible or commercially feasible.

If any of these events occurs, our business and prospects will suffer and the market price of our common stock will likely decline substantially.

Any drugs we develop may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, which could have a material adverse effect on our business.

We intend to sell our products primarily to hospitals which receive reimbursement for the health care services they provide to their patients from third-party payors, such as Medicare, Medicaid and other domestic and international government programs, private insurance plans and managed care programs. Most third-party payors may deny reimbursement if they determine that a medical product was not used in accordance with cost-effective treatment methods, as determined by the third-party payor, or was used for an unapproved indication. Third-party

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payors also may refuse to reimburse for experimental procedures and devices. Furthermore, because our programs are in the early stages of development, we are unable at this time to determine their cost-effectiveness and the level or method of reimbursement. Increasingly, the third-party payors who reimburse patients are requiring that drug companies provide them with predetermined discounts from list prices, and are challenging the prices charged for medical products. If the price we are able to charge for any products we develop is inadequate in light of our development and other costs, our profitability could be adversely affected.

We currently expect that any drugs we develop may need to be administered under the supervision of a physician. Under currently applicable law, drugs that are not usually self-administered may be eligible for coverage by the Medicare program if:

they are incidental to a physician's services,

they are reasonable and necessary for the diagnosis or treatment of the illness or injury for which they are administered according to accepted standard of medical practice,

they are not excluded as immunizations, and

they have been approved by the FDA.

We are subject to intense competition, and we may not compete successfully

We and our strategic partners or licensees may be unable to compete successfully against our current or future competitors. Soft tissue sarcoma patients are typically treated with surgery followed by radiation therapy. Doxorubicin is the only approved drug for treating first-line soft tissue sarcoma and is often used in combination with radiation. In 2012, GlaxoSmithKline's pazopanib was approved for the treatment of patients with advanced soft tissue sarcoma that had received prior chemotherapy. The National Comprehensive Cancer Network also includes the use of ifosfamide, epirubicin, gemcitabine, dacarbazine and liposomal doxorubicin marketed in the U.S. as Doxil by Johnson & Johnson. For patients ineligible for surgery, radiation and/or chemotherapy is the only option. Other approaches to treating soft tissue sarcoma are in late stage clinical development. These include Cell Therapeutics' brostallicin, Sanofi-Aventis' ombrabulin, Threshold Pharmaceuticals' TH-302, trabectedin being co-developed by Johnson & Johnson and PharmaMar and ZIOPHARM Oncology's palifosfamide.

Non-small-cell lung cancer, or NSCLC, is a competitive indication in which patients are treated with a variety of agents. The standard regimen for first-line locally advanced or metastatic NSCLC is a doublet comprised of a platinum agent combined with a taxane, vinka alkaloid or antimetabolite. The addition of Genentech/Roche's Avastin to the standard treatment doublet has resulted significant improvements in survival and rates of remission. Tarceva by Genentech/Roche and Alimta by Eli Lilly & Co. shown benefit for specific NSCLC. In 2011, Pfizer's Xalkori was approved for the treatment of advanced NSCLC patients with a specific and rare gene mutation. In addition, there are several drugs in late-stage development including Eisai's eribulin, Eli Lilly & Co.'s necitumumab, Pfizer's axitinib and Synta Pharmaceuticals' ganetispib.

The pharmaceutical, biopharmaceutical and biotechnology industries are characterized by intense competition and rapid and significant technological advancements. Many companies, research institutions and universities are working in a number of areas similar to our primary fields of interest to develop new products. There also is intense competition among companies seeking to acquire products that already are being marketed. Many of the companies with which we compete have or are likely to have substantially greater research and product development capabilities and financial, technical, scientific, manufacturing, marketing, distribution and other resources than us and at least some of our present or future strategic partners or licensees.

As a result, these competitors may:

succeed in developing competitive products sooner than we or our strategic partners or licensees;

obtain FDA or foreign governmental approvals for their products before we can obtain approval of any of our products;

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obtain patents that block or otherwise inhibit the development and commercialization of our product candidate candidates;

develop products that are safer or more effective than our products;

devote greater resources than we to marketing or selling products;

introduce or adapt more quickly than we to new technologies and other scientific advances;

introduce products that render our products obsolete;

withstand price competition more successfully than we or our strategic partners or licensees;

negotiate third-party strategic alliances or licensing arrangements more effectively than we; and

take better advantage than we of other opportunities.

We will be required to pay substantial milestone and other payments relating to the commercialization of our products.

The agreement relating to our worldwide rights to aldoxorubicin provides for our payment of an aggregate of \$7.5 million upon meeting specified clinical and regulatory milestones up to and including the product's second final marketing approval. We also will be obliged to pay:

commercially reasonable royalties based on a percentage of net sales (as defined in the agreement);

a percentage of non-royalty sub-licensing income (as defined in the agreement); and

milestones of \$1,000,000 for each additional final marketing approval that we might obtain.

The agreements under which we have North American and European rights to tamibarotene provide for our payment of royalties based on net sales of any products, as well as aggregate payments of ¥ 490 million for North America and ¥ 480 million for Europe upon meeting specified clinical, regulatory and sales milestones up to and including the first commercial sale of tamibarotene for the treatment of APL.

Our agreement relating to our worldwide (except Japan) rights to bafetinib provides for our payment of an aggregate of \$13.35 million (including \$5 million upon the product's initial final marketing approval) upon the achievement of specified clinical and regulatory milestones up to and including approvals in the United States and Europe. We also will be obliged to pay:

commercially reasonable royalties based on a percentage of net sales (as defined in the agreement), dependent on reaching certain revenue thresholds;

annual minimum payments if sales of bafetinib do not meet specified levels; and

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a percentage of non-royalty sub-licensing income (as defined in the agreement).

If we are required to pay any third party in order to exercise our rights under the agreement, we will deduct a percentage of those payments from the royalties due under the agreement, up to an agreed-upon cap.

Under the merger agreement by which we acquired Innovive, we agreed to pay the former Innovive stockholders a total of up to approximately \$18.3 million of future earnout merger consideration, subject to our achievement of specified net sales under the Innovive license agreements of aldoxorubicin, tamibarotene and bafetinib. The earnout merger consideration, if any, will be payable in shares of our common stock, subject to specified conditions, or, at our election, in cash or by a combination of shares of our common stock and cash. Our common stock will be valued for purposes of any future earnout merger consideration based upon the trading price of our common stock at the time the earnout merger consideration is paid.

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We are subject to potential liabilities from clinical testing and future product liability claims.

If any of our products are alleged to be defective, they may expose us to claims for personal injury by patients in clinical trials of our products or, if we obtain marketing approval and commercialize our products, by patients using our commercially marketed products. Even if one or more of our products is approved by the FDA, users may claim that such products caused unintended adverse effects. We maintain clinical trial insurance for our ongoing clinical trials, and we plan to seek to obtain similar insurance for any other clinical trials that we conduct. We also would seek to obtain product liability insurance covering the commercial marketing of our product candidates. We may not be able to obtain additional insurance, however, and any insurance obtained by us may prove inadequate in the event of a claim against us. Any claims asserted against us also may divert management's attention from our operations, and we may have to incur substantial costs to defend such claims even if they are unsuccessful.

We may be unable to successfully acquire additional technologies or products. If we require additional technologies or products, our product development plans may change and the ownership interests of our shareholders could be diluted.

We may seek to acquire additional technologies by licensing or purchasing such technologies, or through a merger or acquisition of one or more companies that own such technologies. We have no current understanding or agreement to acquire any technologies, however, and we may not be able to identify or successfully acquire any additional technologies. We also may seek to acquire products from third parties that already are being marketed or have been approved for marketing, although we have not currently identified any of these products. We do not have any prior experience in acquiring or marketing products approved for marketing and may need to find third parties to market any products that we might acquire.

We have focused our product development efforts on our oncology drug candidates, which we believe have the greatest revenue potential. If we acquire additional technologies or product candidates, we may determine to make further changes to our product development plans and business strategy to capitalize on opportunities presented by the new technologies and product candidates.

We may issue shares of our common stock to acquire additional technologies or products or in connection with a merger or acquisition of another company. To the extent we do so, the ownership interest of our stockholders will be diluted accordingly.

We are conducting certain of our clinical trials in foreign countries, which exposes us to additional risks.

We are conducting international clinical development of aldoxorubicin and tamibarotene. The conduct of clinical trials outside the United States could have a significant impact on us. Risks inherent in conducting international clinical trials include:

foreign regulatory requirements that could restrict or limit our ability to conduct our clinical trials;

administrative burdens of conducting clinical trials under multiple foreign regulatory schema;

foreign exchange fluctuations;

diminished protection of intellectual property in some countries; and

possible nationalization and expropriation.

In addition, there may be changes to our business and political position if there is instability, disruption or destruction in a significant geographic region, regardless of cause, including war, terrorism, riot, civil insurrection or social unrest; and natural or man-made disasters, including famine, flood, fire, earthquake, storm or disease, which could seriously harm the development of our current operating strategy.

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In the event of a dispute regarding our international clinical trials, license agreements or other strategic arrangements, it may be necessary for us to resolve the dispute in a foreign country where we would be faced with unfamiliar laws and procedures.

The resolution of disputes in foreign countries can be costly and time consuming, similar to the situation in the United States. However, in a foreign country, we face the additional burden of understanding unfamiliar laws and procedures. We may not be entitled to a jury trial, as we might be in the United States. Further, to litigate in any foreign country, we would be faced with the necessity of hiring lawyers and other professionals who are familiar with the foreign laws. For these reasons, we may incur unforeseen expenses if we are forced to resolve a dispute in a foreign country.

Risks Related to Ownership of Our Common Stock

The market price and trading volume of our common stock may be volatile.

The market price of our common stock could fluctuate significantly for many reasons, including the following factors:

announcements of regulatory developments or technological innovations by us or our competitors,

changes in our relationship with our licensors and other strategic partners,

our quarterly operating results,

developments in patent or other technology ownership rights,

additional funds may not be available on terms that are favorable to us and, in the case of equity financings, may result in dilution to our stockholders,

government regulation of drug pricing, and

general changes in the economy, the financial markets or the pharmaceutical or biotechnology industries.

In addition, factors beyond our control may also have an impact on the price of our common stock. For example, to the extent that other large companies within our industry experience declines in their stock price, our stock price may decline as well. In addition, when the market price of a company's common stock drops significantly, stockholders often institute securities class action lawsuits against the company. A lawsuit against us could cause us to incur substantial costs and could divert the time and attention of our management and other resources.

We may issue preferred stock in the future, and the terms of the preferred stock may reduce the value of our common stock.

We are authorized to issue up to 5,000,000 shares of preferred stock in one or more series. Our board of directors may determine the terms of future preferred stock offerings without further action by our stockholders. If we issue preferred stock, it could affect your rights or reduce the value of our outstanding common stock. In particular, specific rights granted to future holders of preferred stock may include voting rights, preferences as to dividends and liquidation, conversion and redemption rights, sinking fund provisions, and restrictions on our ability to merge with or sell our assets to a third party.

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Anti-takeover provisions of our certificate of incorporation and by-laws and provisions of Delaware law could delay or prevent a change of control that you may favor.

Anti-takeover provisions of our certificate of incorporation and by-laws and provisions of Delaware law may discourage, delay or prevent a merger or other change of control that stockholders may consider favorable, or may impede the ability of the holders of our common stock to change our management. These provisions of our certificate of incorporation and by-laws, among other things:

divide our board of directors into three classes, with members of each class to be elected for staggered three-year terms,

limit the right of stockholders to remove directors,

regulate how stockholders may present proposals or nominate directors for election at annual meetings of stockholders, and

authorize our board of directors to issue preferred stock in one or more series, without stockholder approval.

In addition, Section 203 of the Delaware General Corporation Law provides that, subject to limited exceptions, persons that acquire, or are affiliated with a person that acquires, more than 15% of the outstanding voting stock of a Delaware corporation such as our company shall not engage in any business combination with that corporation, including by merger, consolidation or acquisitions of additional shares for a three-year period following the date on which that person or its affiliate crosses the 15% stock ownership threshold. Section 203 could operate to delay or prevent a change of control of our company.

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

To raise additional capital, we may in the future offer additional shares of our common stock, preferred stock or other securities convertible into or exchangeable for our common stock. We cannot assure you that we will be able to sell shares or other securities in any other offering at a price per share that is equal to or greater than the price per share paid by investors in this offering. The price per share at which we sell additional shares of our common stock or other securities convertible into or exchangeable for our common stock in future transactions may be higher or lower than the price per share in this offering.

Our outstanding options and warrants and the availability for resale of the underlying shares may adversely affect the trading price of our common stock.

As of December 5, 2012, there were outstanding stock options to purchase approximately 1,919,969 shares of our common stock at a weighted-average exercise price of \$5.97 per share and outstanding warrants to purchase approximately 7,677,417 shares of common stock at a weighted-average exercise price of \$5.19 per share. Our outstanding options and warrants could adversely affect our ability to obtain future financing or engage in certain mergers or other transactions, since the holders of options and warrants can be expected to exercise them at a time when we may be able to obtain additional capital through a new offering of securities on terms more favorable to us than the terms of outstanding options and warrants. For the life of the options and warrants, the holders have the opportunity to profit from a rise in the market price of our common stock without assuming the risk of ownership. The issuance of shares upon the exercise of outstanding options and warrants will also dilute the ownership interests of our existing stockholders.

We have registered with the SEC the resale by the holders of all or substantially all shares of our common stock issuable upon exercise of our outstanding options and warrants. The availability of these shares for public resale, as well as any actual resales of these shares, could adversely affect the trading price of our common stock.

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DIVIDEND POLICY

We have never declared or paid cash dividends on our capital stock. We currently intend to retain our future earnings, if any, for use in our business and therefore do not anticipate paying cash dividends in the foreseeable future. Payment of future dividends, if any, will be at the discretion of our board of directors after taking into account various factors, including our financial condition, operating results, and current and anticipated cash needs.

THE SECURITIES THAT WE MAY OFFER

We, directly or through agents, dealers or underwriters designated from time to time, may offer, issue and sell, together or separately, up to \$100,000,000 in the aggregate of:

shares of our common stock, par value \$.001 per share;

shares of our preferred stock, par value \$.01 per share;

warrants to purchase our common stock or preferred stock; and

any combination of the securities listed above, separately or as units, each on terms to be determined at the time of sale.

The common stock, preferred stock, warrants and units collectively are referred to in this prospectus as the securities.

We have summarized below the material terms of the various types of securities that we may offer. We will describe in the applicable prospectus supplement the detailed terms of the securities offered by that supplement. If indicated in the prospectus supplement, the terms of the offered securities may differ from the terms summarized below.

DESCRIPTION OF CAPITAL STOCK

Our authorized capital stock currently consists of 250,000,000 shares of common stock, \$.001 par value per share, and 5,000,000 shares of preferred stock, \$.01 par value per share.

The following summary of certain provisions of our common and preferred stock does not purport to be complete. You should refer to our amended and restated certificate of incorporation and our restated bylaws, which are filed with or incorporated by reference in the registration statement relating to this offering filed by us with the SEC. The summary below is also qualified by reference to the provisions of applicable Delaware corporation law.

Common Stock

Holders of our common stock are entitled to one vote per share on matters on which our stockholders vote, including with respect to the election of directors. Holders of common stock are entitled to receive dividends, if declared by our board of directors, out of funds that we may legally use to pay dividends. See the section of this prospectus entitled "Dividend Policy" for further information. If we liquidate or dissolve, holders of common stock are entitled to share ratably in our assets once our debts and any liquidation preference owed to holders of any then-outstanding preferred stock are paid. No shares of preferred stock will be outstanding immediately after the closing of this offering. All shares of common stock that are outstanding as of the date of this prospectus supplement are, and all shares we are selling in this offering, upon their issuance and sale, will be, fully-paid and nonassessable.

Preferred Stock

We are currently authorized to issue 5,000,000 shares of preferred stock, of which 25,000 shares have been designated as Series A Junior Participating Preferred Stock. We have reserved all of the shares of our Series A Junior Participating Preferred Stock for issuance upon the

exercise of the rights under our Shareholder Protection Rights Agreement described below.

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Our board of directors has the authority to issue shares of preferred stock in one or more series and to fix the rights of each series. These rights may include dividend rights, dividend rates, conversion rights, voting rights, terms of redemption, redemption prices, liquidation preferences, sinking fund terms, and the number of shares that constitute any series. The board of directors may exercise this authority without any further action by our stockholders.

Our board of directors will fix the rights, preferences, privileges, qualifications and restrictions of the preferred stock of each series that we sell under this prospectus in the certificate of designation relating to each such series. We will incorporate by reference as an exhibit to the registration statement of which this prospectus is a part or as an exhibit to one or more current reports on Form 8-K, the form of any certificate of designation that describes the terms of the series of preferred stock we are offering before the issuance of the related series of preferred stock. This description will include:

the title and stated value;

the number of shares we are offering;

the liquidation preference per share;

the purchase price per share;

the dividend rate per share, dividend period, payment date or dates and method of calculation of dividends;

whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;

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

the procedures for any auction and remarketing, if any;

the provisions for a sinking fund, if any;

the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;

any listing of the preferred stock on any securities exchange or market;

whether the preferred stock will be convertible into our common stock or other securities of ours, including warrants, and, if applicable, the conversion price, or how it will be calculated, and under what circumstances and the mechanism by which it may be adjusted, and the conversion period;

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whether the preferred stock will be exchangeable into debt securities or other securities of ours, and, if applicable, the exchange price, or how it will be calculated, and under what circumstances it may be adjusted, and the exchange period;

voting rights, if any;

preemptive rights, if any;

restrictions on transfer, sale or other assignment, if any;

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a discussion of any material United States federal income tax considerations applicable to the preferred stock;

the relative ranking and preferences of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;

any limitations on issuances of any class or series of preferred stock ranking senior or on a parity with the series of preferred stock being issued as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and

any other specific terms, rights, preferences, privileges, qualifications or limitations of, or restrictions on, the preferred stock.

If we issue and sell shares of preferred stock pursuant to this prospectus, the shares will be fully paid and nonassessable and will not have, or be subject to, any preemptive or similar rights.

The laws of the State of Delaware, the state of our incorporation, provide that the holders of preferred stock will have the right to vote separately as a class on any proposal involving fundamental changes in the rights of holders of such preferred stock. This right is in addition to any voting rights that may be provided for in the applicable certificate of designation.

We believe the power to issue preferred stock will provide our board of directors with flexibility in connection with certain possible corporate transactions. The issuance of preferred stock, however, could adversely affect the voting power of holders of our common stock, restrict their rights to receive payment upon liquidation, and have the effect of delaying, deferring, or preventing a change in control which may be beneficial to our stockholders.

Anti-Takeover Measures

Delaware Law

Section 203 of the Delaware General Corporation Law is applicable to takeovers of certain Delaware corporations, including us. Subject to exceptions enumerated in Section 203, Section 203 provides that a corporation shall not engage in any business combination with any interested stockholder for a three-year period following the date that the stockholder becomes an interested stockholder unless:

prior to that date, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;

upon consummation of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, though some shares may be excluded from the calculation; or

on or subsequent to that date, the business combination is approved by the board of directors of the corporation and by the affirmative votes of holders of at least two-thirds of the outstanding voting stock that is not owned by the interested stockholder.

Except as specified in Section 203, an interested stockholder is generally defined to include any person who, together with any affiliates or associates of that person, beneficially owns, directly or indirectly, 15% or more of the outstanding voting stock of the corporation, or is an affiliate or associate of the corporation and was the owner of 15% or more of the outstanding voting stock of the corporation, any time within three years immediately prior to the relevant date. Under certain circumstances, Section 203 makes it more difficult for an interested stockholder to effect various business combinations with a corporation for a three-year period, although the stockholders may elect not to be governed by this section, by adopting an amendment to the certificate of incorporation or by-laws, effective 12 months after adoption. Our amended and restated certificate of incorporation and by-laws do not opt

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out from the restrictions imposed under Section 203. We anticipate that the provisions of Section 203 may encourage companies interested in acquiring us to negotiate in advance with the board because the stockholder approval requirement would be avoided if a majority of the directors then in office excluding an interested stockholder approve either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder. These provisions may have the effect of deterring hostile takeovers or delaying changes in control, which could depress the market price of our common stock and deprive stockholders of opportunities to realize a premium on shares of common stock held by them.

Charter and By-Law Provisions

In addition to the board of directors' ability to issue shares of preferred stock, our amended and restated certificate of incorporation and by-laws contain the following provisions that may have the effect of discouraging unsolicited acquisition proposals:

our by-laws classify the board of directors into three classes with staggered three-year terms;

under our by-laws, our board of directors may enlarge the size of the board and fill the vacancies;

our by-laws provide that a stockholder may not nominate candidates for the board of directors at any annual or special meeting unless that stockholder notifies us of its intention a specified period in advance and provides us with certain required information;

stockholders who wish to bring business before the stockholders at our annual meeting must provide advance notice; and

our by-laws provide that special meetings of stockholders may only be called by our board of directors or by an officer so instructed by our board.

Shareholder Protection Rights Agreement

Our board of directors adopted a Shareholder Protection Rights Agreement, or Rights Agreement, dated April 16, 1997, as amended, between us and American Stock Transfer & Trust Co., as Rights Agent. The Rights Agreement will expire on April 16, 2017, unless renewed or extended by our board of directors. A series of our preferred stock, designated as Series A Junior Participating Preferred Stock, par value \$.01 per share, was created in accordance with the Rights Agreement. The Rights Agreement is designed to deter coercive takeover tactics, including the accumulation of shares in the open market or through private transactions, and to prevent an acquirer from gaining control of us without offering a fair and adequate price and terms to all of our stockholders. As such, the Rights Agreement is intended to enhance our board of directors' ability to protect stockholder interests and help to assure that stockholders receive fair and equal treatment in the event any proposed takeover of CytRx is made in the future. Pursuant to the Rights Agreement, our board of directors declared a dividend distribution of one preferred stock purchase right for each outstanding share of our common stock. The preferred stock purchase rights are attached to, and trade with, our common stock. The purchase rights are exercisable only upon the occurrence of certain triggering events described in the Rights Agreement.

Transfer Agent

The transfer agent for our common stock is American Stock Transfer & Trust Company, 40 Wall Street, New York, New York 10005.

DESCRIPTION OF WARRANTS

We may offer and issue warrants to purchase shares of our common stock or preferred stock. The warrants may be issued independently or as a part of units consisting of shares of our common stock or preferred stock and warrants to purchase additional shares of our common stock or preferred stock. If the warrants are issued pursuant to warrant agreements, we will so specify in the prospectus supplement relating to the warrants being offered pursuant to the prospectus supplement.

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The following description will apply to the warrants offered by this prospectus unless we provide otherwise in the applicable prospectus supplement. The applicable prospectus supplement for a particular series of warrants may specify different or additional terms. The forms of any warrant certificates or warrant agreements evidencing the warrants that we issue will be filed with the SEC and incorporated by reference into this prospectus, and you should carefully review such documents.

The prospectus supplement will describe the following terms of warrants to purchase our common stock, preferred stock or debt securities to the extent applicable:

the title of the warrants;

the common stock or preferred stock for which the warrants are exercisable;

the price at which the warrants will be issued and the exercise price of the warrants;

the aggregate number of warrants offered;

the number of shares of common stock or preferred stock that may be purchased upon the exercise of each warrant;

whether the warrants are being offered separately or as a part of units consisting of shares of our common stock or preferred stock and warrants to purchase additional shares of our common stock or preferred stock;

the terms of any right by us to redeem the warrants;

the date on which the right to exercise the warrants will commence and the date on which this right will expire;

the procedures for exercising the warrants;

the terms on which the warrants may be amended;

the terms of any adjustments in the warrant exercise price and the number of shares of common stock or preferred stock purchasable upon the exercise of each warrant to be made in certain events, including the issuance of a stock dividend to holders of common stock or preferred stock or a stock split, reverse stock split, combination, subdivision or reclassification of common stock;

the effect on the warrants of our merger or consolidation with another entity or our sale of all or substantially all of our assets;

the maximum or minimum number of warrants which may be exercised at any time; and

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the material United States federal income tax consequences applicable to the warrants and their exercise.

Holders of warrants to purchase common stock or preferred stock will not be entitled, by virtue of being such holders, to vote, consent, receive dividends, receive notice as stockholders with respect to any meeting of stockholders for the election of our directors or any other matter, or to exercise any rights whatsoever as our stockholders.

Warrants may be exercised at any time up to the close of business on the expiration date set forth in the prospectus supplement relating to the warrants offered thereby. After the close of business on the expiration date, unexercised warrants will become void. Upon our receipt of the exercise price of the warrants upon the due exercise of the warrants, we will, as soon as practicable, forward the securities purchasable upon exercise. If less than all of the warrants represented by such warrant certificate are exercised, a new warrant certificate will be issued for the remaining warrants.

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DESCRIPTION OF UNITS

We may offer and issue units that consist of shares of our common stock or preferred stock and warrants to purchase additional shares of our common stock or preferred stock. For example, we may elect to issue units for a specified price per unit, with each unit consisting of one share of our common stock or preferred stock and one warrant to purchase an additional share of our common stock or preferred stock at a specified price. The holder of a unit will also hold each of the securities that is included in the unit.

We have provided in the preceding sections of this prospectus a general description of our common stock, preferred stock, and debt securities and of the warrants that we may offer. If we elect to offer units, we will describe the specific terms of the units in a supplement to this prospectus. Among other things, the prospectus supplement will describe, to the extent applicable:

the price of each unit;

the securities comprising each unit;

the exercise price of the warrants comprising part of the units;

the aggregate number of units offered;

the number of shares of common stock or preferred stock that may be purchased upon the exercise of each warrant comprising part of a unit;

the terms of any right by us to redeem any of the securities comprising the units;

the date on which the right to exercise the warrants forming part of the units will commence and the date on which this right will expire;

any transfer restrictions on the units, including whether the securities comprising the units may be transferred separately;

the terms on which the units or warrants forming part of the units may be amended;

with respect to preferred stock forming part of the units, the other matters listed above under **Description of Capital Stock - Preferred Stock** ;

with respect to warrants forming part of the units, the other matters listed above under **Description of Warrants** ; and

the material United States federal income tax consequences applicable to the units.

PLAN OF DISTRIBUTION

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We may sell the securities being offered hereby in one or more of the following ways from time to time:

through agents to the public or to investors;

to one or more underwriters for resale to the public or to investors;

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in at the market offerings, within the meaning of Rule 415(a)(4) of the Securities Act of 1933, as amended, or the Securities Act, to or through a market maker or into an existing trading market, on an exchange or otherwise;

directly to investors; or

through a combination of these methods of sale.

We will set forth in a prospectus supplement the terms of an offering of shares of our securities, including.

the name or names of any agents or underwriters;

the purchase price of the securities being offered and the proceeds we will receive from the sale;

any over-allotment options under which underwriters may purchase additional securities from us;

any agency fees or underwriting discounts and other items constituting agents or underwriters compensation;

the public offering price; and

any discounts or concessions allowed or reallocated or paid to dealers.

We may distribute the securities from time to time in one or more transactions;

at a fixed price or prices, which may be changed;

at market prices prevailing at the time of sale;

at prices related to such prevailing market prices; or

at negotiated prices.

We may also, from time to time, authorize dealers, acting as our agents, to offer and sell securities upon the terms and conditions set forth in the applicable prospectus supplement. We, or the purchasers of securities for whom the underwriters may act as agents, may compensate underwriters in the form of underwriting discounts or commissions, in connection with the sale of securities. Underwriters may sell the securities to or through dealers, and those dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters or commissions from the purchasers for whom they may act as agent. Unless otherwise indicated in a prospectus supplement, an agent will be acting on a best efforts basis and a dealer will purchase securities as a principal, and may then resell the common stock at varying prices to be determined by the dealer.

We will describe in the applicable prospectus supplement any compensation we will pay to underwriters or agents in connection with the offering of securities, and any discounts, concessions or commissions allowed by underwriters to participating dealers. The dealers and agents

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participating in the distribution of securities may be deemed to be underwriters, and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions. We may enter into agreements to indemnify underwriters, dealers and agents against certain civil liabilities, including liabilities under the Securities Act and to reimburse these persons for certain expenses. We may grant underwriters who participate in the distribution of securities we are offering under this prospectus an option to purchase additional shares to cover over-allotments, if any, in connection with the distribution.

To facilitate the offering of 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

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making purchases in the open market or by exercising their over-allotment option, if any. In addition, these persons may stabilize or maintain the price of the securities by bidding for or purchasing securities in the open market or by imposing penalty bids, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if securities sold by them is 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.

Any underwriters who are qualified market makers on the Nasdaq Capital Market may engage in passive market making transactions in the securities on the Nasdaq Capital Market in accordance with Rule 103 of Regulation M, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded.

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

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at <http://www.sec.gov>. The SEC's website contains reports, proxy and information statements and other information regarding issuers such as us that file electronically with the SEC. You may also read and copy any document we file with the SEC at the SEC's Public Reference Room at 100 F Street, N.E., Room 1580, Washington, D.C. 20549, and may obtain copies of these documents at prescribed rates by writing to the SEC. Please call the SEC at 1-800-SEC-0330 for further information on the operation of its Public Reference Room.

Information about us is also available at our website at www.cytrx.com; however, information on our website is not incorporated into this prospectus and is not a part of this prospectus.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to incorporate by reference the information we have filed with it, which means that we can disclose important information to you by referring you to another document that we have filed separately with the SEC. You should read the information incorporated by reference because it is an important part of this prospectus. Any statement in a document we incorporate by reference into this prospectus will be considered to be modified or superseded to the extent a statement contained in this prospectus or any other subsequently filed document that is incorporated by reference into this prospectus modifies or supersedes that statement. The modified or superseded statement will not be considered to be a part of this prospectus, except as modified or superseded.

We incorporate by reference the following information or documents that we have filed with the SEC (excluding those portions of any Form 8-K that are not deemed filed pursuant to the General Instructions of Form 8-K):

our Annual Report on Form 10-K for the year ended December 31, 2011;

our Quarterly Reports on Form 10-Q for the quarterly periods ended March 31, 2012, June 30, 2012, and September 30, 2012, respectively;

our Current Reports on Form 8-K filed with the SEC on January 6, 2012, February 17, 2012, February 21, 2012, April 23, 2012, May 10, 2012, May 15, 2012, October 19, 2012 and November 9, 2012, respectively;

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the description of our securities as described in our Registration Statement on Form 8 A filed under the Exchange Act on March 17, 1987 (File No. 0 15327), and any amendment or report filed for the purpose of updating any such description; and

the description of our Series A Junior Participating Preferred Stock Purchase Rights as described in our Registration Statement on Form 8 A filed under the Exchange Act on April 17, 1997 (File No. 000 15327), and any amendment or report filed for the purpose of updating any such descriptions.

We also incorporate by reference all documents filed pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus and prior to the termination of this offering (excluding those portions of any Form 8-K that are not deemed filed pursuant to the General Instructions of Form 8-K).

Statements made in this prospectus or in any document incorporated by reference in this prospectus as to the contents of any contract or other document referred to herein or therein are not necessarily complete, and in each instance reference is made to the copy of such contract or other document filed as an exhibit to the documents incorporated by reference, each such statement being qualified in all material respects by such reference.

You may obtain a copy of the foregoing documents from us without charge by writing or calling us at the following address and telephone number: 11726 San Vicente Blvd., Suite 650 Los Angeles, California 90049, Attention: Corporate Secretary; (310) 826-5648.

LEGAL MATTERS

The validity of the securities being offered hereby has been passed upon for us by TroyGould PC, Los Angeles, California. As of November 30, 2012, TroyGould PC owned 7,000 shares of our common stock.

EXPERTS

The consolidated financial statements and schedules as of December 31, 2011 and 2010 and for each of the three years in the period ended December 31, 2011 and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2011 incorporated by reference in this prospectus have been so incorporated in reliance on the reports of BDO USA, LLP, an independent registered public accounting firm, incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

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PROSPECTUS

\$100,000,000

The date of this prospectus is , 2012

Table of Contents**PART II****INFORMATION NOT REQUIRED IN PROSPECTUS****ITEM 14. OTHER EXPENSES OF ISSUANCE AND DISTRIBUTION**

We estimate that the expenses incurred in connection with the distribution described in this registration statement will be as set forth below. We will bear all of such expenses.

| | |
|------------------------------------|------------------|
| SEC registration fee | \$ 13,640 |
| Transfer agent fees and expenses | \$ 2,000 |
| Nasdaq Capital Market listing fees | * |
| FINRA corporate filing fees | \$ 15,500 |
| Accounting fees and expenses | \$ 10,000 |
| Legal fees and expenses | \$ 30,000 |
| Printing expenses | \$ 20,000 |
| Miscellaneous | \$ 5,000 |
| Total | \$ 96,140 |

* Estimated expenses, if any, not presently known.

ITEM 15. INDEMNIFICATION OF DIRECTORS AND OFFICERS

Section 102(b)(7) of the Delaware General Corporation Law authorizes a corporation in its certificate of incorporation to eliminate or limit personal liability of directors of the corporation for violations of the directors' fiduciary duty of care. However, directors remain liable for breaches of duties of loyalty, failing to act in good faith, engaging in intentional misconduct, knowingly violating a law, paying a dividend or approving a stock repurchase which was illegal under Delaware General Corporation Law Section 174 or obtaining an improper personal benefit. In addition, equitable remedies for breach of fiduciary duty of care, such as injunction or recession, are available.

Our certificate of incorporation eliminates the personal liability of the members of our board of directors to the fullest extent permitted by law. Specifically, Article Eleven of our certificate of incorporation provides as follows:

A director of the corporation shall not be personally liable to the corporation or its stockholders for monetary damages for breach of fiduciary duty as a director, except for liability (i) for any breach of the director's duty of loyalty to the corporation or its stockholders, (ii) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (iii) under Section 174 of the Delaware General Corporation Law, or (iv) for any transaction from which the director derived any improper personal benefit. If the Delaware General Corporation Law is amended after approval by the stockholders of this Article to authorize corporate action further eliminating or limiting the personal liability of directors, then the liability of a director of the corporation shall be eliminated or limited to the fullest extent permitted by the Delaware General Corporation Law as so amended.

Any repeal or modification of the foregoing paragraph by the stockholders of the corporation shall not adversely affect any right or protection of a director of the corporation existing at the time of such repeal or modification.

In addition, our certificate of incorporation and bylaws provide for indemnification of our officers and directors to the fullest extent permitted by law. In particular, Article Nine of our certificate of incorporation provides as follows:

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The corporation shall, to the fullest extent permitted by Section 145 of the General Corporation Law of the State of Delaware, as the same may be amended and supplemented, indemnify any and all persons whom it shall have power to indemnify under said section from and against any and all of the expenses, liabilities or other matters referred to in or covered by said section, and the indemnification provided for herein shall not be deemed exclusive of any other rights to which those indemnified may be entitled under any bylaw, agreement, vote of stockholders or disinterested directors or otherwise, both as to action in his official capacity and as to action in another capacity while holding such office, and shall continue as to a person who has ceased to be a director, officer, employee or agent and shall inure to the benefit of the heirs, executors and administrators of such a person.

Section 145 of the Delaware General Corporation Law empowers a corporation to indemnify any person who was or is party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative, by reason of the fact that he is or was a director, officer or agent of the corporation or another enterprise if serving at the request of the corporation. Depending on the character of the proceeding, a corporation may indemnify against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding if the person indemnified acted in good faith in respect to any criminal action or proceeding, had no reasonable cause to believe his conduct was unlawful. In the case of an action by or in the right of the corporation, no indemnification may be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or the court in which such action or suit was brought shall determine that despite the adjudication of liability such person is fairly and reasonably entitled to indemnity for such expenses which the court shall deem proper. Section 145 further provides that to the extent a director, officer, employee or agent of a corporation has been successful in the defense of any action, suit or proceeding referred to above or in the defense of any claim, issue or matter therein, he shall be indemnified against expenses (including attorneys' fees) actually and reasonably incurred by him in connection therewith. Our bylaws permit it to purchase insurance on behalf of such person against any liability asserted against him and incurred by him in any such capacity, or arising out of his status as such, whether or not we would have the power to indemnify him against such liability under the foregoing provision of the bylaws.

We hold an insurance policy covering directors and officers under which the insurer agrees to pay, with some exclusions, for any claim made against our directors and officers for a wrongful act that they may become legally obligated to pay or for which we are required to indemnify our directors or officers.

Insofar as indemnification for liabilities arising under the Securities Act of 1933, as amended, or the Securities Act, may be permitted for directors, officers and controlling persons of the Company under the above provisions, or otherwise, the Commission has advised us that, in its opinion, such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Company of expenses incurred or paid by a director, officer or controlling person of the Company in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Company will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

ITEM 16. EXHIBITS

The exhibits listed in the accompanying Exhibit Index are filed or incorporated by reference as part of this registration statement.

ITEM 17. UNDERTAKINGS.

(a) The undersigned registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

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- (i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;
- (ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement; notwithstanding the foregoing, any increase or decrease in the volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Securities and Exchange Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20 percent change in the maximum aggregate offering price set forth in the Calculation of Registration Fee table in the effective registration statement; and
- (iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement; provided, however, that paragraphs (a)(1)(i), (a)(1)(ii) and (a)(1)(iii) of this section do not apply if the registration statement is on Form S-3 and the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Securities and Exchange Commission by the registrant pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.
- (2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
- (3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.
- (4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:
- (i) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and
- (ii) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof; provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is a part of the registration statement will, as to a purchaser with a time of contract sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was a part of the registration statement or made in any such document immediately prior to such effective date.
- (5) That, for the purpose of determining liability of the registrant under the Securities Act of 1933 to any purchaser in the initial distribution of securities, the undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:

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- (i) Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;
- (ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;
- (iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and
- (iv) Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.
- (b) The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934 and (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
- (c) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act of 1933 and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act of 1933 and will be governed by the final adjudication of such issue.
- (d) The undersigned registrant hereby undertakes that:
- (1) For purposes of determining any liability under the Securities Act of 1933, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act of 1933 shall be deemed to be part of this registration statement as of the time it was declared effective; and
- (2) For the purpose of determining any liability under the Securities Act of 1933, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

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Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Registration Statement on Form S-3 to be signed on its behalf by the undersigned, thereunto duly authorized in the City of Los Angeles, State of California, on December 5, 2012.

CYTRX CORPORATION

By: /s/ STEVEN A. KRIEGSMAN
 Steven A. Kriegsman
 President and Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Steven A. Kriegsman as his true and lawful attorney-in-fact and agent, with full power of substitution, for him and in his name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this registration statement on Form S-3, and to sign any registration statement for the same offering covered by this registration statement that is to be effective upon filing pursuant to Rule 462(b) promulgated under the Securities Act of 1933, and all post-effective amendments thereto, and to file the same and all prospectus supplements, with all exhibits thereto and all documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorney-in-fact and agent full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent, or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed by the following persons in the capacities and on the dates indicated:

| Signature | Title | Date |
|--|---|------------------|
| /s/ STEVEN A. KRIEGSMAN Steven A. Kriegsman | President and Chief Executive Officer and Director | December 5, 2012 |
| /s/ JOHN Y. CALOZ John Y. Caloz | Chief Financial Officer and Treasurer (principal financial and accounting officer) | December 5, 2012 |
| /s/ LOUIS J. IGNARRO Louis J. Ignarro, Ph.D | Director | December 5, 2012 |
| /s/ MAX LINK Max Link | Director | December 5, 2012 |
| /s/ JOSEPH RUBINFELD Joseph Rubinfeld, Ph.D | Director | December 5, 2012 |
| /s/ MARVIN R. SELTER Marvin R. Selter | Director | December 5, 2012 |
| /s/ RICHARD L. WENNEKAMP | Director | December 5, 2012 |

Richard L. Wennekamp

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Table of Contents**EXHIBIT INDEX**

The following exhibits are filed herewith or incorporated by reference:

Exhibit

| Number | Description |
|---------------|---|
| 1.1 | Form of Underwriting Agreement.* |
| 3.1 | Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to the Registrant's Annual Report on Form 10-K filed on April 1, 2008). |
| 3.2 | Restated By-Laws (incorporated by reference to Exhibit 4.2 to the Registrant's Registration Statement on Form S-8 (File No. 333-37171) filed on July 21, 1997). |
| 4.1 | Shareholder Protection Rights Agreement dated April 16, 1997 between CytRx Corporation and American Stock Transfer & Trust Company as Rights Agent (incorporated by reference to Exhibit 99.1 to the Registrant's Current Report on Form 8-K filed April 17, 1997). |
| 4.2 | Amendment No. 1 to Shareholder Protection Rights Agreement (incorporated by reference to Exhibit 4.2 to the Registrant's Annual Report on Form 10-K filed on April 1, 2002). |
| 4.3 | Amendment No. 2 to Shareholder Protection Rights Agreement (incorporated by reference to Exhibit 4.3 to the Registrant's Annual Report on Form 10-K filed on April 2, 2007). |
| 4.4 | Form of Preferred Stock Certificate.* |
| 4.5 | Certificate of Designation regarding the rights, preferences, privileges and restrictions with respect to any preferred stock issued under this registration statement.* |
| 4.6 | Form of Warrant Agreement for Common Stock, including form of Warrant.* |
| 4.7 | Form of Warrant Agreement for preferred stock, including form of Warrant.* |
| 4.8 | Form of Unit Certificate.* |
| 5.1 | Opinion of TroyGould PC. |
| 23.1 | Consent of TroyGould PC (included in Exhibit 5.1). |
| 23.2 | Consent of BDO USA, LLP. |
| 24.1 | Power of Attorney (included on Page II-5). |

* To be filed, if applicable, subsequent to the effectiveness of this registration statement (1) by an amendment to this registration statement or (2) as an exhibit to a Current Report on Form 8-K and incorporated herein by reference.