

CYTRX CORP  
Form 424B5  
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Registration No. 333-170437

The information in this preliminary prospectus supplement is not complete and may be changed. A registration statement relating to these securities became effective under the Securities Act of 1933, as amended. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities, and we are not soliciting an offer to buy these securities, in any jurisdiction where the offer or sale is not permitted.

**PRELIMINARY PROSPECTUS SUPPLEMENT SUBJECT TO COMPLETION DATED OCTOBER 17, 2012**

**(To the Prospectus dated December 14, 2010)**

## Shares

### Common Stock

We are offering \_\_\_\_\_ shares of our common stock, par value \$0.001 per share, pursuant to this prospectus supplement and the accompanying prospectus.

Our common stock is listed on The NASDAQ Capital Market under the symbol CYTR. On October 16, 2012, the last reported sale price of our common stock on The NASDAQ Capital Market was \$3.52 per share.

**Our business and an investment in our common stock involve significant risks. See Risk Factors beginning on page S-8 of this prospectus supplement and on page 3 of the accompanying prospectus.**

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

	Per Share	Total
Public offering price	\$	\$

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Underwriting discount <sup>(1)</sup>	\$	\$
Proceeds, before expenses, to us	\$	\$

<sup>(1)</sup>The underwriters will receive compensation in addition to the underwriting discount. See Underwriting beginning on page S-21 of this prospectus supplement for a description of the compensation payable to the underwriters. The underwriters may also purchase up to an additional shares from us at the public offering price, less the underwriting discount, within 30 days from the date of this prospectus supplement to cover over-allotments, if any.

The underwriters expect to deliver the shares against payment therefor on or about , 2012.

*Sole Book-Running Manager*

**Aegis Capital Corp**

, 2012

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**PROSPECTUS**

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### **ABOUT THIS PROSPECTUS SUPPLEMENT**

This document is part of the registration statement that we filed with the Securities and Exchange Commission (the SEC) using a shelf registration process and consists of two parts. The first part is this prospectus supplement, including the documents incorporated by reference, which describes the specific terms of this offering. The second part, the accompanying prospectus, including the documents incorporated by reference, gives more general information, some of which may not apply to this offering. Generally, when we refer only to the prospectus, we are referring to both parts of this document combined. This prospectus supplement may add to, update or change information in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement or the accompanying prospectus.

If information in this prospectus supplement is inconsistent with the accompanying prospectus or with any document incorporated by reference that was filed with the SEC before the date of this prospectus supplement, you should rely on this prospectus supplement. This prospectus supplement, the accompanying prospectus and the documents incorporated into each by reference include important information about us, the securities being offered and other information you should know before investing in our securities. You should also read and consider information in the documents we have referred you to in the section of this prospectus supplement and the accompanying prospectus entitled **Where You Can Find More Information**.

You should rely only on this prospectus supplement, the accompanying prospectus and any free writing prospectus we may provide to you in connection with this offering and the information incorporated or deemed to be incorporated by reference therein. We have not authorized anyone to provide you with information that is in addition to or different from that contained or incorporated by reference in this prospectus supplement and the accompanying prospectus. If anyone provides you with different or inconsistent information, you should not rely on it. We are not offering to sell these securities in any jurisdiction where the offer or sale is not permitted. You should not assume that the information contained or incorporated by reference in this prospectus supplement or the accompanying prospectus is accurate as of any date other than as of the date of this prospectus supplement or the accompanying prospectus, as the case may be, or in the case of the documents incorporated by reference, the date of such documents regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or any sale of our securities. Our business, financial condition, liquidity, results of operations and prospects may have changed since those dates.

No action has been or will be taken in any jurisdiction by us or the underwriters that would permit a public offering of the common stock or the possession or distribution of this prospectus supplement and the accompanying prospectus in any jurisdiction, other than in the United States. Persons outside the United States who come into possession of this prospectus supplement and the accompanying prospectus must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus supplement and the accompanying prospectus outside the United States. This prospectus supplement and the accompanying prospectus do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

In this prospectus supplement and in the accompanying prospectus, we sometimes refer to CytRx Corporation as CytRx, to our former subsidiary, RXi Pharmaceuticals Corporation, as RXi, and to our former subsidiary, Innovive Pharmaceuticals, Inc., which we acquired in September 2008 and merged into CytRx in December 2010, as Innovive. References in this prospectus supplement and in the accompanying prospectus 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 supplement or in the accompanying prospectus may include forward-looking statements that reflect our current views with respect to our ongoing and planned clinical trials, 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 similar 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 supplement and in the accompanying prospectus and under the captions Risk Factors, 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 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 shares of common stock, you should consider carefully all of the factors set forth or referred to in this prospectus supplement and in the accompanying prospectus that could cause actual results to differ.

## SUMMARY

*This summary highlights selected information about us, this offering and information appearing elsewhere in this prospectus supplement or in the accompanying prospectus or incorporated by reference in this prospectus supplement and the accompanying prospectus. This summary is not complete and does not contain all of the information that may be important to you and that you should consider before purchasing our shares. This prospectus supplement and the accompanying prospectus include or incorporate by reference information about our shares, as well as information regarding our business and detailed financial data. Before making an investment decision, to fully understand this offering and its consequences to you, you should carefully read this entire prospectus supplement and the accompanying prospectus, including Risk Factors beginning on page S-8 of this prospectus supplement and page 3 of the accompanying prospectus, and the financial statements, related notes and other information that we incorporated by reference herein, including our Annual Report on Form 10-K for the fiscal year ended December 31, 2011.*

## The Company

### Overview

We are a biopharmaceutical research and development company specializing in oncology. Our oncology pipeline includes two programs in clinical development for cancer indications: aldorubicin (formerly known as INNO-206) and tamibarotene. With our tumor-targeted doxorubicin conjugate aldorubicin, 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 aldorubicin in combination with doxorubicin in patients with advanced solid tumors. We plan to meet with the Food and Drug Administration ( FDA ) in the fourth quarter of 2012 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. 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.

### Recent Developments

On May 16, 2012, we effected a 1-for-7 reverse stock split of our outstanding shares of common stock and our common stock began trading on The NASDAQ Capital Market on a split-adjusted basis.

### Our Product Candidate Pipeline

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

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

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.

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.

#### ***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-g 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 RARa, 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 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/m<sup>2</sup>/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 1 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.

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 supplement or the accompanying prospectus the information on, or accessible through, our website, and you should not consider it as part of this prospectus supplement or the accompanying prospectus.

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**The Offering**

Securities offered by us	shares of common stock
Common stock to be outstanding after this offering	shares of common stock
Use of proceeds	We intend to use the net proceeds of this offering to fund the clinical development of aldoxorubicin and tamibarotene and for general corporate purposes, which may include working capital, capital expenditures, research and development expenditures and other commercial expenditures. See Use of Proceeds on page S-18 for further information.
Risk factors	See Risk Factors beginning on page S-8 of this prospectus supplement and page 3 of the accompanying prospectus for a discussion of factors you should read and consider carefully before investing in our common stock.
NASDAQ Capital Market symbol	CYTR
Except as otherwise indicated, all information in this prospectus supplement:	

based on 21,217,370 shares outstanding on October 16, 2012;

assumes no exercise by the underwriters of their over-allotment option to purchase up to an additional \_\_\_\_\_ shares to cover over-allotments, if any;

excludes 1,919,969 shares of our common stock subject to options outstanding as of October 16, 2012 having a weighted-average exercise price of \$5.97 per share;

excludes 4,107,376 shares of our common stock that have been reserved for issuance in connection with future grants under our stock option plans as of October 16, 2012; and

excludes 7,677,417 shares of our common stock that have been reserved for issuance upon exercise of outstanding warrants as of October 16, 2012 having a weighted-average exercise price of \$5.19 per share.

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## 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 into this prospectus supplement and the accompanying 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. Please also see page 3 of the accompanying prospectus for additional risk 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 \$13.3 million for the six months ended June 30, 2012. We had an accumulated deficit as of June 30, 2012 of \$234.3 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.

***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 six months ended June 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 June 30, 2012, we had cash and cash equivalents of approximately \$11.9 million and marketable securities of approximately \$15.1 million. Management believes that our current resources along with the net proceeds of this offering will be sufficient to fund our operations for the foreseeable future. The belief is based in part upon our currently estimated expenditures for 2012 of approximately \$23.7 million, which includes approximately \$7.0 million for our clinical programs for aldorubicin, approximately \$5.3 million for our clinical program for tamibarotene, approximately \$0.4 million for our clinical programs for bafetinib, approximately \$4.5 million for general operation of our clinical programs, and approximately \$6.5 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.

***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 aldorubicin, 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;

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

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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.

***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.

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.

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***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 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.