CYTRX CORP
Form 424B5
January 30, 2014
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Filed Pursuant to Rule 424(b)(5)
Registration No. 333-185308

**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.**

SUBJECT TO COMPLETION, DATED JANUARY 30, 2014

**PRELIMINARY PROSPECTUS SUPPLEMENT**
(To Prospectus dated December 21, 2012)

# Shares

# Common Stock

We are offering shares of our common stock. Our common stock is listed on The NASDAQ Capital Market under the symbol CYTR. On January 29, 2014, the last reported sale price of our common stock on The NASDAQ Capital Market was $7.36 per share.

**Investing in our common stock involves a high degree of risk. Please read Risk Factors beginning on page S-9 of this prospectus supplement, on page 8 of the accompanying prospectus and in the documents incorporated by reference into this prospectus supplement.**

**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 | $ | $ |
| Underwriting Discounts and Commissions[(1)] | $ | $ |
| Proceeds to CytRx Corporation before expenses | $ | $ |

(1) We have agreed to reimburse the underwriters for certain expenses. See Underwriting.

Delivery of the shares of common stock is expected to be made on or about , 2014. We have granted the underwriters an option for a period of 30 days to purchase an additional shares of our common stock. If the underwriters exercise the option in full, the total underwriting discounts and commissions payable by us will be $ , and the total proceeds to us, before expenses, will be $ .

*Sole Book-Running Manager*

**Jefferies**

Prospectus Supplement dated January , 2014

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**PROSPECTUS SUPPLEMENT**



**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, or 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 sections 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 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 2008, 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.

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## 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 an 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 supplement and the accompanying prospectus. 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.

## INDUSTRY DATA

Unless otherwise indicated, information contained or incorporated by reference in this prospectus supplement or the accompanying prospectus concerning our industry, including our general expectations and market opportunity, is based on information from our own management estimates and research, as well as from industry and general publications and research, surveys and studies conducted by third parties. Management estimates are derived from publicly available information, our knowledge of our industry and assumptions based on such information and knowledge, which we believe to be reasonable. In addition, assumptions and estimates of our and our industry s future performance are necessarily subject to a high degree of uncertainty and risk due to a variety of factors, including those described in Risk Factors beginning on page S-9 of this prospectus supplement and on page 8 of the accompanying prospectus. These and other factors could cause our future performance to differ materially from our assumptions and estimates.

## TRADEMARKS

CytRx is one of our trademarks used in this prospectus supplement and the accompanying prospectus. This prospectus supplement and the accompanying prospectus also include trademarks, trade names and service marks that are the property of other organizations. Solely for convenience, trademarks and trade names referred to in this prospectus supplement and the accompanying prospectus sometimes appear without the ® and symbols, but those references are not intended to indicate that we will not assert, to the fullest extent under applicable law, our rights, or that the applicable owner will not assert its rights, to these trademarks and trade names.

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## SUMMARY

*This summary highlights selected information about us, this offering and information contained or incorporated by reference in this prospectus supplement or in 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-9 of this prospectus supplement and page 8 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, 2012 and our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2013, June 30, 2013 and September 30, 2013.*

### The Company

***Overview***

We are a biopharmaceutical research and development company specializing in oncology. We currently are focused on the clinical development of aldoxorubicin (formerly known as INNO-206), our modified version of the widely-used chemotherapeutic agent, doxorubicin. We recently reported top-line and hazard ratio results of our Phase 2b clinical trial with aldoxorubicin as a treatment for soft tissue sarcoma, or STS. Hazard ratios - the likelihood that the study endpoint (in this case tumor progression) will be reached during a given period - are an important measure of the reliability and uniformity of the absolute data for progression-free survival, or PFS. The trial investigated the efficacy and safety of aldoxorubicin compared with doxorubicin in subjects with first-line metastatic, locally advanced or unresectable STS. Aldoxorubicin combines the chemotherapeutic agent doxorubicin with a novel linker-molecule that binds specifically to albumin in the blood to allow for delivery of higher amounts of doxorubicin (3½ to 4 times) without the major dose-limiting toxicities seen with administration of doxorubicin alone.

In the first quarter of 2014, we plan to initiate a pivotal Phase 3 trial of aldoxorubicin as a therapy for patients with STS whose tumors have progressed following treatment with chemotherapy. The Phase 3 trial is expected to be conducted under a Special Protocol Assessment, or SPA, granted by the U.S. Food and Drug Administration, or FDA. The SPA means that the FDA agrees that the design and analyses proposed in the Phase 3 trial protocol are acceptable to support regulatory approval of the product candidate with respect to effectiveness of the indication studied, and will not subsequently change its perspective on these matters, unless previously unrecognized public or animal health concerns were to arise or we subsequently modify the protocol. Thus, if the study demonstrates an acceptable benefit-risk profile as determined by the FDA, it would suffice as the single pivotal trial to demonstrate effectiveness and would support registration of aldoxorubicin for this indication.

We have initiated a Phase 2 clinical trial with aldoxorubicin in patients with AIDS-related Kaposi s sarcoma. We have completed a Phase 1b study of aldoxorubicin in combination with doxorubicin in patients with advanced solid tumors and a Phase 1b pharmacokinetics clinical trial in patients with metastatic solid tumors. We have initiated a Phase 2 clinical trial with aldoxorubicin in patients with recurrent glioblastoma (brain cancer).

We plan to expand our pipeline of oncology candidates based on a linker platform technology that can be utilized with multiple chemotherapeutic agents and may allow for greater concentration of drug at tumor sites. We also have rights to two additional drug candidates, tamibarotene and bafetinib. We completed our evaluation of bafetinib in the ENABLE Phase 2 clinical trial in high-risk B-cell chronic lymphocytic leukemia and are seeking a partner for any further development of bafetinib. We ceased our Phase 2b clinical trial of tamibarotene in patients with non-small-cell lung cancer after it failed to show efficacy.

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***Our Product Candidate Pipeline***

The following table summarizes aldoxorubicin s current or impending stages of development:

| TECHNOLOGY | PRODUCT CANDIDATE | INDICATIONS | STAGE OF DEVELOPMENT |
|---|---|---|---|
| Doxorubicin conjugate | Aldoxorubicin | Soft tissue sarcoma | Phase 3 1Q14<br>Phase 2b ongoing |
| | | Glioblastoma multiforme | Phase 2 ongoing |
| | | Kaposi s sarcoma | Phase 2 ongoing |

***Our Clinical Development Programs***

Our clinical development programs are summarized below:

*Aldoxorubicin*

Aldoxorubicin is a conjugate of the commonly prescribed chemotherapeutic agent doxorubicin that binds to circulating albumin in the bloodstream and is concentrated at the site of tumors. Specifically, it is comprised of (6-Maleimidocaproyl) hydrazine, an acid-sensitive molecule that is conjugated to doxorubicin. We plan to intiate under an SPA granted by the FDA a pivotal Phase 3 trial of aldoxorubicin as a therapy for patients with STS whose tumors have progressed following treatment with chemotherapy.

*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, ovarian 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 mouth and digestive tract), stomatitis (inflammation of soft tissue of the mouth), and necrotizing extravasation (damage due to the leakage of intravenous drugs from the vein into the surrounding tissue).

We believe aldoxorubicin has attributes that may improve on doxorubicin, alone, which we sometimes refer to as native doxorubicin, including the potential to reduce several of the adverse events, improve efficacy and achieve increased concentration at tumor sites.

Our postulated 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 gastrointestinal tract due to a mechanism called Enhanced Permeability and Retention by Solid Tumors ;
- once albumin-bound aldoxorubicin is taken up by the tumor, the acidic environment within the tumor and in the cancer cells themselves causes cleavage of the acid-sensitive linker; and
- free doxorubicin is then 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. Toxicology studies in rodents also demonstrated a reduction in cardiotoxicity. Animal studies conducted by aldoxorubicin inventor Dr. Felix Kratz of the 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.

We also recently announced additional data from a study of aldoxorubicin in immunodeficient mice transplanted with human glioblastoma cells in their brain that showed those animals treated with aldoxorubicin had a median survival rate of more than 63 days, compared with approximately 25 days for animals treated

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with doxorubicin or saline. The data also indicated evidence of drug concentration inside tumors growing in the brain, but not in normal brain tissue, and significant tumor regression in aldoxorubicin-treated animals, while doxorubicin did not appear to enter the tumor or brain to any significant degree and showed little or no efficacy in the treatment of these brain tumors. Aldoxorubicin significantly reduced the number of dividing cells within the brain tumors in this trial and showed a statistically relevant increased expression of apoptosis or cell death markers.

*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 the types of side effects compared with those historically observed with native doxorubicin. Of 35 evaluable patients, 23 had either an objective clinical (partial) response or stable disease. Objective clinical responses were observed in patients with STS, breast and small cell lung cancers.

We completed a Phase 1b/2 clinical trial with aldoxorubicin in patients with advanced solid tumors who had either relapsed or failed to respond to their prior chemotherapy 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) was shown in ten of 13 (76.9%) evaluable patients with relapsed or refractory STS. The median number of cycles of aldoxorubicin administered at the maximum tolerable dose was eight.

In addition, best responses for the 13 evaluable STS trial subjects included the following: five (38.5%) achieved partial response, as defined as shrinkage of target tumors 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 PFS for advanced STS patients in the trial was approximately 6.4 months with a range of 1.0 to more than 10.7 months.

In connection with our Phase 1b pharmacokinetics clinical trial evaluating the pharmacokinetics and safety of aldoxorubicin in patients with metastatic solid tumors who have either relapsed or not responded to treatment with standard therapies, we announced data demonstrating that aldoxorubicin has a distribution half-life of approximately 20 to 24 hours, with a narrow volume of distribution to healthy tissue and slow clearance from the circulation. These characteristics distinguish aldoxorubicin from doxorubicin, which has a distribution half-life of about five minutes according to its package insert.

In December 2011, we initiated our Phase 2b clinical trial to evaluate the preliminary efficacy and safety of aldoxorubicin as a first-line therapy in patients with advanced STS who are ineligible for surgery. The Phase 2b clinical trial provided the first direct clinical trial comparison of aldoxorubicin and native doxorubicin, which is dose-limited due to toxicity, as a first-line therapy.

The Phase 2b clinical trial with aldoxorubicin in patients with STS is an international trial in 31 treatment centers under the direction of Sant P. Chawla, M.D., F.R.A.C.P., Director of the Sarcoma Oncology Center in Santa Monica, California. The Phase 2b clinical trial s primary objectives are to measure the PFS, tumor response and overall survival of patients with advanced STS 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.

In our 123-subject clinical trial, subjects with advanced STS were administered either 350 mg/m$^2$ of aldoxorubicin (83 subjects) or 75 mg/m$^2$ of doxorubicin (40 subjects) every three weeks for up to six cycles. Subjects were followed every six weeks with CT scans to monitor tumor size. The primary endpoint was PFS as determined by a blinded radiology review performed at an independent central radiology laboratory. Secondary

endpoints included overall response rates (complete and partial) and PFS at six months for each group, and overall survival, which will be reported when the clinical trial is complete.

The central radiology review, as well as the investigators own assessments, showed an 80% to 100% improvement in PFS among patients treated with aldoxorubicin. In an intent-to-treat analysis, the investigator-assessed median PFS was 8.4 months for aldoxorubicin patients versus 4.7 months for doxorubicin patients (p=0.0002), while the blinded central radiology review indicated that median PFS for aldoxorubicin patients was 5.7 months versus 2.8 months for doxorubicin patients (p=0.018). Per investigators, 67.1% of aldoxorubicin patients had not progressed at six months, compared with 36.1% of doxorubicin-treated patients (p=0.008). By blinded central radiology review, 46.8% of aldoxorubicin patients had not progressed at six months, compared with 23.7% of doxorubicin patients (p=0.038).

The overall response rate as determined by the investigators was 24.0% for aldoxorubicin subjects (2.7% complete response and 21.3% partial response) versus 5.3% for doxorubicin subjects (0% complete response and 5.3% partial response). As assessed by blinded central review, 23.0% of aldoxorubicin subjects had a partial response while none of the doxorubicin subjects exhibited any objective response.

Additional analysis determined hazard ratios for the primary endpoint of PFS by both investigators at study sites and by a blinded radiology review. The hazard ratio for investigator-read scans is 0.37 (95% confidence interval, range of 0.212 to 0.643) (p=0.0004), reflecting a 63% reduction in the risk of disease progression; and the hazard ratio for central lab scans is 0.586 (95% confidence interval, range of 0.358 to 0.960) (p=0.034), reflecting a 41% reduction in the risk of disease progression. Hazard ratios are an important measure of the reliability and uniformity of the data for PFS, and where the upper limit is less than one indicate that there is a significant difference between the two study groups.

We also reported that a Kaplan-Meier analysis of the trial results, which analysis describes the time it takes for tumors to progress in individual patients, showed significant improvement in subjects treated with aldoxorubicin versus subjects treated with doxorubicin. We expect to present full study results for this clinical trial later this year.

In the Phase 2b clinical trial, aldoxorubicin was found to be safe and well tolerated. All adverse events in subjects treated with aldoxorubicin were consistent with the known side effects of doxorubicin, resolved before the administration of the next dose and did not require treatment discontinuation. There were no treatment-related deaths in the aldoxorubicin group.

In the first quarter of 2014, we plan to initiate a pivotal Phase 3 trial of aldoxorubicin as a therapy for patients with STS whose tumors have progressed following treatment with chemotherapy under an SPA granted by the FDA. The Phase 3 clinical trial s primary endpoint will be PFS. The trial also will assess overall survival, objective tumor response and safety. We expect to enroll approximately 400 patients in the trial.

We have begun patient dosing in a Phase 2 clinical trial to evaluate the preliminary efficacy and safety of aldoxorubicin in patients with unresectable glioblastoma whose tumors have progressed following prior treatment with surgery, radiation and with the drug temozolomide. The clinical trial is expected to eventually enroll approximately 28 patients at sites including the John Wayne Cancer Center in Santa Monica, California, City of Hope in Duarte, California, and the LSU Medical Center in New Orleans, Louisiana.

We have initiated a Phase 2 clinical trial evaluating the preliminary efficacy of aldoxorubicin in patients with AIDS-related Kaposi s sarcoma, a common HIV-associated tumor. The current standard-of-care for severe dermatological and systemic Kaposi s sarcoma is liposomal doxorubicin (Doxil); however, a significant proportion of patients exhibit minimal or no clinical response to this agent, and the drug s toxicity often prevents continued therapy. The Phase 2 trial will enroll up to 30 patients and is being conducted at the LSU Medical Center in New Orleans, Louisiana.

In 2012, we completed a Phase 2 trial for patients with advanced pancreatic ductal adenocarcinomas who had relapsed or failed to respond to two prior regimens, one regimen containing gemcitabine (Gemzar) and the

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other a fluoropyrimidine such as 5-fluorouracil. No objective clinical responses were observed in 14 patients treated with native aldoxorubicin, and we are considering testing the aldoxorubicin in combination with the commonly-prescribed drug Abraxane as a second-line treatment in that indication.

*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. 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. We hold rights to bafetinib in all territories, except in Japan.

We plan to seek a partner for any further development of bafetinib in order to focus our resources on the development of aldoxorubicin.

*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, a component of the current first-line treatment for acute promyelocytic leukemia, or APL.

We ceased our Phase 2b clinical trial of tamibarotene in patients with non-small-cell lung cancer after it failed to show efficacy.

***Financial Condition***

As of December 31, 2013, we had cash and cash equivalents of approximately $11.5 million and short-term investments of approximately $27.1 million.

***Reverse Stock Split***

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. All share and per share amounts in this prospectus supplement have been adjusted to reflect the reverse stock split as if it had occurred at the beginning of the earliest period presented.

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

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**THE OFFERING**

| | |
|---|---|
| Common Stock 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 our clinical trials of aldoxorubicin and for general corporate purposes, which may include working capital, capital expenditures, research and development and other commercial expenditures. See Use of Proceeds on page S-18 for further information. |
| Risk factors | See Risk Factors beginning on page S-9 of this prospectus supplement and page 8 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 is:

- based on 30,608,392 shares outstanding on September 30, 2013;
- assumes no exercise by the underwriters of their option to purchase up to an additional shares of our common stock;
- excludes 3,406,881 shares of our common stock subject to options outstanding as of September 30, 2013, having a weighted-average exercise price of $4.15 per share;
- excludes 7,595,701 shares of our common stock that have been reserved for issuance in connection with future grants under our stock option plans as of September 30, 2013; and
- excludes 8,083,181 shares of our common stock that have been reserved for issuance upon exercise of outstanding warrants as of September 30, 2013, having a weighted-average exercise price of $4.91 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 8 of the accompanying prospectus for additional risk factors.*

**Risks Associated With Our Business**

***We have operated at a loss and will 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 approximately $18.0 million for the year ended December 31, 2012 and of approximately $20.3 million for the nine months ended September 30, 2013, and had an accumulated deficit as of September 30, 2013 of approximately $249.2 million. We will continue to incur losses unless and until we are able to commercialize aldoxorubicin or one or more of our other current or future 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 aldoxorubicin and our other 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 revenue was $100,000 for the year ended December 31, 2012 and $200,000 for the nine months ended September 30, 2013. We will have no significant recurring revenue unless we are able to commercialize aldoxorubicin, our lead product candidate, or one of our preclinical candidates, either of which may require us to first enter into strategic arrangements with third parties.

At December 31, 2013, we had cash and cash equivalents of approximately $11.5 million and short-term investments of approximately $27.1 million. Management believes that our current cash and cash equivalents and short-term investments, together with the net proceeds of this

offering, will be sufficient to fund our operations for the foreseeable future. These expectations are based upon numerous assumptions and subject to many uncertainties, and our actual experience may be significantly different from these expectations.

If we obtain marketing approval and successfully commercialize aldoxorubicin or other product candidate, 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

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revenue. Our ability to raise capital may be adversely affected by the 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 projected development goals in the time frames we estimate, the commercialization of our products may be delayed and our business prospects may suffer. Our financial projections 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 clinical development programs.

We also may disclose projected expenditures or other forecasts for future periods. These and other financial projections 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 forecasting.

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. The assumptions management has used to produce these projections may significantly change or prove to be inaccurate. Accordingly, you should not unduly rely on any of these financial projections.

***The regulatory approval process is lengthy, time consuming and inherently unpredictable, and 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, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate s clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate.

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.

On October 1, 2013, the U.S. federal government suspended services deemed non-essential as a result of the failure by Congress to enact regular appropriations for the 2014 fiscal year. Although the impasse has been resolved until at least January 2014, if another similar or more prolonged shutdown were to occur, it could result in significant delays in the FDA s ability to timely review and process any submissions we have filed or may file, or cause other regulatory delays affecting our development or commercial operations, which delays could have a material adverse effect on our business.

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. In addition, even if we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our products, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

Furthermore, even if we obtain regulatory approvals, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, import, export, advertising, promotion and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with current good manufacturing practices, or cGMPs, and good clinical practices, or cGCPs, for any clinical trials that we conduct post-approval. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market, or voluntary or mandatory product recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or our strategic partners, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; and
- injunctions or the imposition of civil or criminal penalties.

The FDA s policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business. We will also be subject to periodic inspections and the potential for mandatory post- approval clinical trials required 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.

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***Clinical drug development involves a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results. Our current and planned clinical trials of our lead product candidate may fail to show that it is clinically safe and effective, or that it is better than alternative treatments.***

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. Product candidates in later stages of clinical development may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or safety profiles, notwithstanding promising results in earlier trials. For example, aldoxorubicin has shown encouraging preliminary clinical results in our Phase 1b/2 clinical trial and in top-line PFS data from our Phase 2b clinical trial of aldoxorubicin as a treatment for STS; however, these conclusions may not be reproduced in future clinical trial results, including the final data from the Phase 2b clinical trial or the planned Phase 3 clinical trial testing aldoxorubicin as a treatment for STS. 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 for any indication.

Further, we may experience delays in clinical trials of our product candidates. We do not know whether ongoing clinical trials will be completed on schedule or at all, or whether planned clinical trials will begin on time, need to be redesigned, enroll patients on time or be completed on schedule, if at all. Clinical trials can be delayed for a variety of reasons, including delays related to:

- obtaining regulatory approval to commence a trial;
- reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- obtaining institutional review board approval at each clinical trial site;
- recruiting suitable patients to participate in a trial;
- having patients complete a trial or return for post-treatment follow-up;
- clinical trial sites deviating from trial protocol or dropping out of a trial;
- adding new clinical trial sites; or
- manufacturing sufficient quantities of product candidate for use in clinical trials.

Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, competing clinical trials and clinicians and patients perceptions as to the potential advantages of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating. Furthermore, we rely on third parties, such as CROs and clinical trial sites, to ensure the proper and timely conduct of our clinical trials and while we have agreements governing their committed activities, we have limited influence over their actual performance.

We could encounter delays if prescribing physicians encounter unresolved ethical issues associated with enrolling patients in clinical trials of our product candidates in lieu of prescribing existing treatments that have established safety and efficacy profiles. Further, a clinical trial may be suspended or terminated by us, our collaborators, the institutional review boards, or IRBs, if the institutions in which such trials are being

conducted, the Data Safety Monitoring Board for such trial, or by the FDA or other regulatory authorities due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. If we experience delays in the completion of, or termination of, any clinical trial of our product candidates, the commercial prospects of our product candidates will be harmed, and our ability to generate product revenues from any of these product candidates will be delayed. In addition, any delays in completing our clinical trials will increase

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our costs, slow down our product development and approval process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may harm our business, financial condition and prospects significantly. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

***Our SPA with the FDA for our pivotal study of aldoxorubicin does not guarantee marketing approval in the United States.***

We have an SPA with the FDA for the pivotal trial of aldoxorubicin for the treatment of STS. The SPA means that the FDA agrees that the design and analyses proposed in a protocol are acceptable to support regulatory approval of the product candidate with respect to effectiveness of the indication studied, and will not subsequently change its perspective on these matters, unless a previously unrecognized public or animal health concern were to arise or we subsequently modify the protocol. Even under an SPA, marketing approval by the FDA is not guaranteed, because a final determination that the agreed-upon protocol satisfies a specific objective, such as the demonstration of efficacy and safety (positive benefit-risk ratio), or supports an approval decision, will be based on a complete review of all the data submitted to the FDA.

***Adverse side effects or other safety risks associated with our product candidates could delay or preclude approval, cause us to suspend or discontinue clinical trials, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.***

Undesirable side effects caused by our product candidates could result in the delay, suspension or termination of our clinical trials by us, our collaborators, IRBs, the FDA or other regulatory authorities. If we elect or are required to delay, suspend or terminate any clinical trial of any product candidates that we develop, the commercial prospects of such product candidates will be harmed and our ability to generate product revenues from any of these product candidates will be delayed or eliminated. Any of these occurrences may harm our business, financial condition and prospects significantly.

To date, patients treated with aldoxorubicin have experienced some of the same drug-related side effects associated with doxorubicin, including myelosuppression (decreased production of blood cells by bone marrow), gastrointestinal disorders (nausea and vomiting), mucositis (inflammation of the mucous membranes lining the digestive tract, including the mouth), stomatitis (inflammation of the mouth s soft tissue), fatigue, fever and other signs of infection associated with neutropenia (an abnormally low count of a type of white blood cells) and alopecia (hair loss). Results of our trials could reveal an unacceptable incidence of these or other side effects. In such an event, our trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. In addition, the drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

Furthermore, if we or others later identify undesirable side effects caused by the product, a number of potentially significant negative consequences could result, including: