

CYTRX CORP
Form S-3
November 27, 2013
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As filed with the Securities and Exchange Commission on November 27, 2013

Reg. No. 333-

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM S-3

REGISTRATION STATEMENT

UNDER

THE SECURITIES ACT OF 1933

CYTRX CORPORATION

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

CytRx Corporation

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

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11726 San Vicente Boulevard, Suite 650

Los Angeles, California 90049

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

Steven A. Kriegsman

President and Chief Executive Officer

CytRx Corporation

11726 San Vicente Boulevard, Suite 650

Los Angeles, California 90049

(310) 826-5648

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

With copies to:

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

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

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

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

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

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

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

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

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

CALCULATION OF REGISTRATION FEE

Title of each class of securities to be registered	Amount to be registered	Proposed maximum offering price per share	Proposed maximum aggregate offering price	Amount of registration fee
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Common stock, par value \$.001 per share	6,440,045 shares(1)(2)	\$4.48(3)	\$28,851,402(3)	\$ 3,717
Common stock, par value \$.001 per share(2)	(2)(4)			
Preferred stock, \$.01 par value per share(4)	(4)			
Warrants(4)(5)	(4)			
Units(4)(5)	(4)			
Subtotal			\$100,000,000(5)	\$12,880(6)
Total			\$128,851,402	\$16,597(6)

- (1) Represents shares issuable upon exercise of outstanding warrants. In accordance with Rule 416, there is also being registered hereunder such indeterminate number of additional shares of common stock as may become issuable upon exercise of the warrants to prevent dilution resulting from stock splits, stock dividends or similar transactions.
- (2) Each share of common stock will be accompanied by one Series A Junior Participating Preferred Stock Purchase Right that trades with the common stock. The value, if any, attributable to this right is reflected in the market price of common stock. Prior to the occurrence of certain events, none of which has occurred as of the date of this registration statement, the rights will not be exercisable or evidenced separately from the common stock.
- (3) The price is estimated in accordance with Rule 457(g) under the Securities Act of 1933 solely for the purpose of calculating the registration fee and represents the exercise price of the warrants.

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- (4) Pursuant to Rule 457(o) under the Securities Act of 1933 and General Instruction II.D to Form S-3 under the Securities Act of 1933, the number of shares, warrants or units is not specified. There is being registered hereunder an indeterminate amount of common stock, preferred stock, warrants and units of the registrant as may from time to time be issued at indeterminate prices. The maximum offering price per class of securities will be determined from time to time by the registrant in connection with the issuance of the securities. However, in no event will the maximum aggregate offering price of the securities issued exceed \$100,000,000 or such lesser aggregate amount permitted under General Instruction I.B.6 to Form S-3 under the Securities Act of 1933. Pursuant to Rule 416 under the Securities Act of 1933, this registration statement also registers such indeterminate amounts of securities as may be issued upon conversion of, or in exchange for, the securities registered hereunder and such indeterminate number of shares of common stock and preferred stock as may be issued from time to time upon conversion or exchange as a result of stock splits, stock dividends or similar transactions.
- (5) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(o) under the Securities Act of 1933.
- (6) Pursuant to Rule 415(a)(6) under the Securities Act of 1933, \$27,764,800 of the securities registered by this registration statement consists of unsold securities previously registered under the registration statement on Form S-3 (Reg. No. 333-170437) declared effective on December 14, 2010. Pursuant to Rule 457(p) under the Securities Act of 1933, the registration fee of \$1,979 paid with respect to such unsold securities in connection with such previous registration statement is offset against the filing fee due hereunder.

THE REGISTRANT HEREBY AMENDS THIS REGISTRATION STATEMENT ON SUCH DATE OR DATES AS MAY BE NECESSARY TO DELAY ITS EFFECTIVE DATE UNTIL THE REGISTRANT SHALL FILE A FURTHER AMENDMENT WHICH SPECIFICALLY STATES THAT THIS REGISTRATION STATEMENT SHALL THEREAFTER BECOME EFFECTIVE IN ACCORDANCE WITH SECTION 8(A) OF THE SECURITIES ACT OF 1933 OR UNTIL THIS REGISTRATION STATEMENT SHALL BECOME EFFECTIVE ON SUCH DATE AS THE COMMISSION, ACTING PURSUANT TO SAID SECTION 8(A), MAY DETERMINE.

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EXPLANATORY NOTES

This Registration Statement contains two prospectuses, as described below:

a prospectus relating to up to 6,440,045 shares of common stock of the registrant issuable upon the exercise of outstanding August 2011 warrants of the registrant; and

a prospectus relating to up to \$100,000,000 of securities of the registrant that the registrant may offer and sell in one or more transactions utilizing the shelf registration process described in the prospectus.

The two prospectuses are substantively identical, except for the following principal differences:

they contain different outside front covers and back covers;

the August 2011 warrants prospectus refers throughout to the registrant's offer and sale of shares of common stock issuable upon the August 2011 warrants, and the shelf registration prospectus refers throughout to the registrant's offer and sale of its common stock, preferred stock and warrants, either separately, together or as units, described in the prospectus;

the August 2011 warrants prospectus has additional risk factors in the Risk Factors Associated with Our Common Stock section relating to dilution and to management's discretion as to the use of proceeds of the offering under the August 2011 warrants prospectus;

the August 2011 warrants prospectus contains a Dilution section;

the two prospectuses contain different Use of Proceeds sections;

the shelf registration prospectus also contains a Financial Ratio section, while the August 2011 warrants prospectus does not;

the two prospectuses contain different Plan of Distribution sections; and

the August 2011 warrants prospectus contains a description of the August 2011 warrants in the Description of Capital Stock section and the shelf registration prospectus contains The Securities That We May Offer, Description of Capital Stock, Description of Warrants and Description of Units sections.

The registrant has included in this registration statement, after the prospectus relating to the August 2011 warrants, the shelf registration prospectus, which prospectus reflects the foregoing principal differences from the August 2011 warrants prospectus.

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

SUBJECT TO COMPLETION, DATED NOVEMBER 27, 2013

PROSPECTUS

6,440,045 Shares of Common Stock

Issuable Upon Exercise of August 2011 Warrants

This prospectus relates to shares of our common stock issuable upon the exercise of our outstanding August 2011 warrants. The August 2011 warrants were offered and sold by us pursuant to a prospectus supplement dated July 27, 2011 and a related base prospectus dated December 13, 2010. The prospectus supplement and base prospectus also covered the offer and sale by us of the shares of our common stock underlying the August 2011 warrants. The ongoing offer for sale by us of the shares of our common stock issuable upon exercise of the August 2011 warrants is being made pursuant to this prospectus. The August 2011 warrants are exercisable until August 1, 2016 at a current exercise price of \$4.48 per share of our common stock, subject to adjustment in events specified in the August 2011 warrants.

Our common stock is traded on The NASDAQ Capital Market under the symbol CYTR. On November 26, 2013, the closing sale price of our common stock on The NASDAQ Capital Market was \$2.3799.

An investment in our common stock involves a high degree of risk. See Risk Factors beginning on page A-7 of this prospectus.

NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED OF THESE SECURITIES OR PASSED UPON THE ADEQUACY OR ACCURACY OF THIS PROSPECTUS. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

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The date of this prospectus is _____, 2013.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or the SEC. As permitted by the rules and regulations of the SEC, the registration statement filed by us includes additional information not contained in this prospectus. You may read the registration statement and the other reports we file with the SEC at the SEC's web site or its offices described under the heading "Where You Can Find More Information" in this prospectus.

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

NOTE ON FORWARD-LOOKING STATEMENTS

Some of the statements contained or incorporated by reference in this 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 forward-looking nature identify forward-looking statements for purposes of the federal securities laws or otherwise.

All forward-looking statements involve inherent risks and uncertainties, and there are or will be important factors that could cause actual results to differ materially from those indicated in these statements. We believe that these factors include, but are not limited to, those factors set forth under the caption "Risk Factors" in this prospectus and 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 most recent Quarterly Report on Form 10-Q, all of which you should review carefully. Please consider our forward-looking statements in light of those risks as you read this prospectus. 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 our 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 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 A-7 of this 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. This prospectus also includes 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 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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Table of Contents**PROSPECTUS SUMMARY**

This summary highlights selected information appearing elsewhere in this prospectus or incorporated by reference in this prospectus and does not contain all of the information that may be important to you or that you should consider before investing in our common stock. This prospectus includes or incorporates by reference information about the securities we are offering, as well as information regarding our business and detailed financial data. Before making an investment decision, you should read this prospectus and the information incorporated by reference herein in their entirety, including Risk Factors beginning on page A-6 of this prospectus.

The Company**Overview**

We are a biopharmaceutical research and development company specializing in oncology. We currently are focused on the clinical development of aldorubicin (formerly known as INNO-206), our modified version of the widely-used chemotherapeutic agent, doxorubicin. We are conducting a global Phase 2b clinical trial with aldorubicin as a treatment for soft tissue sarcoma, have completed a Phase 1b/2 clinical trial primarily in the same indication, a Phase 1b study of aldorubicin in combination with doxorubicin in patients with advanced solid tumors, and a Phase 1b pharmacokinetics clinical trial in patients with metastatic solid tumors. We plan to initiate under a Special Protocol Assessment, or SPA, granted by the U.S. Food and Drug Administration, or FDA, a potential pivotal Phase 3 global trial of aldorubicin as a therapy for patients with soft tissue sarcoma whose tumors have progressed following treatment with chemotherapy. We also have initiated a Phase 2 clinical trial with aldorubicin in patients with late-stage glioblastoma (brain cancer), and will be initiating a Phase 2 clinical trial with aldorubicin in patients with AIDS-related Kaposi's sarcoma. 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 (B-CLL), plan to seek a partner for further development of bafetinib.

Our Product Candidate Pipeline

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

	Product		Stage of
Technology	candidate	Indication(s)	development
Doxorubicin conjugate	Aldorubicin	Soft tissue sarcoma	Phase 3 1Q14
		Glioblastoma multiforme	Phase 2b ongoing
		Kaposi's sarcoma	Phase 2 ongoing
		In combination with doxorubicin in patients with advanced solid tumors	Phase 2 4Q13
			Phase 1b complete

Our Clinical Development Programs

Our current 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 the (6-Maleimidocaproyl) hydrazone of doxorubicin attached to an acid-sensitive linker known as EMCH. We are initiating a potential pivotal Phase 3 global trial of aldoxorubicin as a therapy for patients with soft tissue sarcoma whose tumors have progressed following treatment with chemotherapy under an SPA granted by the FDA. The SPA means that the FDA agrees with the design, execution and analyses proposed in the Phase 3 trial protocol and will not subsequently change its perspective on these matters, unless previously unrecognized public or animal health concerns were to arise. It also means that if the study demonstrates the acceptable benefit-risk profile as described in the protocol, it would suffice as the single pivotal trial that would likely support registration of aldoxorubicin for this indication.

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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 mouth and digestive tract), stomatitis (inflammation of soft tissue of the mouth), and extravasation (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 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 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. 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 with doxorubicin or saline. The data also indicated evidence of drug concentration inside tumors growing in the brain and significant tumor regression in aldoxorubicin-treated animals, while doxorubicin did not appear to enter the tumor 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. Twenty-three of thirty-five 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 ten of 13 (76.9%) evaluable patients with relapsed or refractory soft tissue sarcoma.

In addition, best responses for the 13 evaluable soft tissue sarcoma 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 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.

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In 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 recently announced data demonstrating that aldoxorubicin has a circulating half-life of approximately 20 to 24 hours, with narrow volume of distribution to healthy tissue and slow clearance from the circulation. These characteristics distinguish aldoxorubicin from published pharmacokinetics data for doxorubicin.

Development Plan. We plan to initiate under a SPA granted by the FDA a potential pivotal Phase 3 global trial with aldoxorubicin as a therapy for patients with soft tissue sarcomas whose tumors have progressed following treatment with chemotherapy. The Phase 3 clinical trial's primary endpoint will be progression-free survival. The trial also will assess overall survival, objective tumor response and safety. We expect to enroll approximately 400 patients, commencing in the first quarter of 2014.

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 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 soft tissue sarcoma is an international trial 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 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.

Preliminary data based on the first 82 evaluated patients in the Phase 2b clinical trial showed that aldoxorubicin-treated patients demonstrated a significantly greater percentage of overall responses compared with those treated with doxorubicin, the current standard-of-care for advanced, metastatic soft-tissue sarcoma. This was based on a blinded reading of tumor scans by an independent radiology review. We expect to report in December 2013 final, top-line data for the global Phase 2b clinical trial, including data related to the trial's primary endpoint of progression-free survival.

We have initiated 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 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 also plan to initiate in 2013 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 will be 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 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, 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, or CLL. 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 adoxorubicin.

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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 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.

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

The Offering

The August 2011 warrants were sold and issued in our public offering completed on August 1, 2011. See the Plan of Distribution section in this prospectus for more information regarding this offering.

Issuer	CytRx Corporation
Shares offered by us	6,440,045 shares of our common stock issuable upon exercise of our outstanding August 2011 warrants
Shares outstanding	41,975,412 shares (excluding treasury shares) as of November 26, 2013, excluding 5,050,017 shares subject to outstanding stock options and warrants (other than the August 2011 warrants)
Shares outstanding following this offering	48,415,457 shares (excluding treasury shares) assuming all August 2011 warrants are exercised in full and without giving effect to any other issuances of common stock subsequent to November 26, 2013
Use of proceeds	We intend to use the net proceeds of any exercises of the August 2011 warrants pursuant to this offering to augment our working capital and for general corporate purposes
Trading	Our common stock is traded on The NASDAQ Capital Market under the symbol CYTR

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RISK FACTORS

You should carefully consider the risks described below before deciding whether to exercise the August 2011 warrants. 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. 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, including our financial statements and related notes. We have attempted to identify below the major factors that could cause differences between actual and planned or expected results, but we cannot assure you that we have identified all such factors.

Risks Associated With Our Business

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 September 30, 2013, we had cash and cash equivalents of approximately \$6.0 million and short-term investments of \$17.0 million. Management believes that our current cash and cash equivalents and short-term investments, including the net proceeds of approximately \$24.1 million from our public offering completed on October 15, 2013, 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 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.

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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.

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.

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.

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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 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 lead product candidate may fail to show that it is clinically safe and effective, or that it is better than alternative treatments.

Aldoxorubicin has shown encouraging preliminary clinical results in our Phase 1b/2 clinical trial and in preliminary data from our Phase 2b clinical trial of aldoxorubicin as a treatment for soft tissue sarcomas; however, these conclusions may not be reproduced in future clinical trial results, including the final, top-line data from the Phase 2b clinical trial or the planned global Phase 3 clinical trial testing aldoxorubicin as a treatment for soft tissue sarcomas.

Top-line data from our Phase 2b clinical trial of aldoxorubicin as a treatment for soft tissue sarcomas may differ from our recently announced preliminary data. Even if our current trials are successful, subsequent trials may not yield statistically significant data indicating that aldoxorubicin is 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 for any indication.

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 soft-tissue sarcomas. The SPA means that the FDA agrees with the design, execution, and analyses proposed in a protocol, and constitutes a commitment that the FDA will not subsequently change its perspectives on these matters, unless a previously unrecognized public or animal health concern were to arise or changes were to be made to the protocol, itself. Even under a 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.

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

We do not have the facilities or expertise to manufacture supplies of aldoxorubicin or any of our other 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. However, we have no supply arrangements for the commercial manufacture of this product candidate 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 aldoxorubicin, our lead product candidate, or our other 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 any of our products that are approved for marketing cannot be

manufactured at an acceptable cost, the commercial success of such product candidates 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 or our other product candidates, as well as marketing and commercialization, may require us to enter into strategic alliances or other collaborative arrangements with other pharmaceutical companies under which those companies will be responsible for one or more aspects of the eventual marketing and commercialization of our products.

Our products, if approved for marketing, 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.

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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 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 and other product candidates, 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.

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.

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Any products 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 that may be approved for marketing 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. For patients ineligible for surgery, radiation and/or chemotherapy is the only option. Doxorubicin is the only approved drug for treating soft tissue sarcoma patients who are ineligible for surgery and is often used in combination with radiation. The National Comprehensive Cancer Network also includes the use of ifosfamide, epirubicin, gemcitabine, dacarbazine and liposomal doxorubicin marketed in the United States as Doxil by Johnson & Johnson. GlaxoSmithKline's Votrient was approved in the United States and Europe in 2012 for the treatment of advanced soft tissue sarcomas following prior chemotherapy. There are other approaches to treating soft tissue sarcoma in late-stage clinical development, including Threshold Pharmaceuticals' TH-302 and trabectedin being co-developed by Johnson and Johnson and PharmaMar.

Patients with glioblastoma multiforme (GBM) generally undergo invasive brain surgery, although disease progression following surgery is nearly 100%. The front-line therapy for GBM following surgery is Temozolomide (Temodar®) in combination with radiation. Bevacizumab (Avastin®) has been approved for the treatment of GBM in patients

failing Temodar®. Drugs in development to treat GBM include rindopepimut by Celldex Therapeutics, DCVax by Northwest Biotherapeutics, TRC105 from Tracoon Pharmaceuticals, and buparlisib by Novartis. Kaposi's sarcoma is generally treated with radiation, surgery and/or liposomal doxorubicin. Other drugs in development for Kaposi's sarcoma include selumetinib by AstraZeneca and pomalidamide by Celgene.

Many companies, including large pharmaceutical and biotechnology firms with financial resources, research and development staffs, and facilities that may be substantially greater than those of ours or our strategic partners or licensees, are engaged in the research and development of pharmaceutical products that could compete with our potential products. To the extent that we seek to acquire, through license or otherwise, existing or potential new products, we will be competing with numerous other companies, many of which will have substantially greater financial resources, large acquisition and research and development staffs that may give those companies a competitive advantage over us in identifying and evaluating these drug acquisition opportunities. Any products that we acquire will be competing with products marketed by companies that in many cases will have substantially greater marketing resources than we have. The industry is characterized by rapid technological advances and competitors may develop their products more rapidly and such products may be more effective than those currently under development or that may be developed in the future by our strategic partners or licensees. Competitive products for a number of the disease indications that we have targeted are currently being marketed by other parties, and additional competitive products are under development and may also include products currently under development that we are not aware of or products that may be developed in the future.