CYTRX CORP
Form 424B5
July 20, 2015
Table of Contents

**Filed Pursuant to Rule 424(b)(5)**
**Registration No. 333-192597**

**THE INFORMATION IN THIS PRELIMINARY PROSPECTUS SUPPLEMENT AND THE ACCOMPANYING PROSPECTUS IS NOT COMPLETE AND MAY BE CHANGED. THIS PRELIMINARY PROSPECTUS SUPPLEMENT AND THE ACCOMPANYING PROSPECTUS ARE NOT AN OFFER TO SELL THESE SECURITIES AND ARE NOT SOLICITING AN OFFER TO BUY THESE SECURITIES IN ANY STATE OR OTHER JURISDICTION WHERE THE OFFER OR SALE IS NOT PERMITTED.**

SUBJECT TO COMPLETION, DATED JULY 20, 2015

**PRELIMINARY PROSPECTUS SUPPLEMENT**

(To Prospectus dated December 23, 2013)

**Shares**

**Common Stock**

We are offering shares of our common stock. Each share of our common stock to be offered and sold is accompanied by one Series A Junior Participating Preferred Stock Purchase Right that trades with our common stock. Our common stock is listed on The NASDAQ Capital Market under the symbol CYTR. On July 17, 2015, the closing price of our common stock on The NASDAQ Capital Market was $3.97 per share.

**Investing in our common stock involves a high degree of risk. Please read Risk Factors beginning on page S-12 of this prospectus supplement, on page B-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 July , 2015. 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 July , 2015

Table of Contents

# TABLE OF CONTENTS

## PROSPECTUS SUPPLEMENT



## PROSPECTUS

Table of Contents

## 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 t CytRx, alone, unless otherwise indicated.

S-1

Table of Contents

## 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, shou will and similar statements of a future or forward-looking nature identify forward-looking statements for purposes of the federal securities laws or otherwise.

All forward-looking statements involve inherent risks and uncertainties, and there are or will be important factors that could cause actual results to differ materially from those indicated in these statements. We believe that these factors include, but are not limited to, those factors set forth under the caption Risk Factors in this prospectus supplement and in the accompanying prospectus and under the captions Risk Factors, Business, Legal Proceedings, Management s Discussion and Analysis of Financial Condition and Results of Operations, Quantitative and Qualitative Disclosures About Market Risk and Controls and Procedures in our most recent Annual Report on Form 10-K and Quarterly Report on Form 10-Q, all of which you should review carefully. Please consider our forward-looking statements in light of those risks as you read this prospectus 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.

Table of Contents

## 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-12 of this prospectus supplement and on page B-8 of the accompanying prospectus. These and other factors could cause our future performance to differ materially from our assumptions and estimates.

Table of Contents

## TRADEMARKS

CytRx and LADR are 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.

Table of Contents

## 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-12 of this prospectus supplement and page B-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, 2014 and our Quarterly Report on Form 10-Q for the quarter ended March 31, 2015.*

### The Company

***Overview***

We are a biopharmaceutical research and development company specializing in oncology. We are currently focused on the clinical development of aldoxorubicin (formerly known as INNO-206), our modified version of the widely-used chemotherapeutic agent, doxorubicin. We previously reported positive top-line efficacy results (median progression-free survival, or PFS, PFS at six months, overall response rates, hazard ratios and overall survival) from our completed, global Phase 2b clinical trial with aldoxorubicin as a treatment for soft tissue sarcoma, or STS. Hazard ratios, or 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 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 and is designed to allow for delivery of higher amounts of doxorubicin (3 ½ to 4 times) without the major dose-limiting toxicities as seen with the administration of doxorubicin alone.

In the first quarter of 2014, we initiated 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 being conducted under a Special Protocol Assessment, or SPA, granted by the 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 change its perspective on these matters, except in limited circumstances such as where a sponsor fails to follow a protocol agreed to with the FDA or where previously unrecognized health concerns occur. Thus, if the study demonstrates an acceptable benefit-risk profile as determined by the FDA, it will support registration of aldoxorubicin for this indication. If approved for marketing, our current plan would be to commercially launch aldoxorubicin in late 2017.

We are currently evaluating aldoxorubicin in a global Phase 2b clinical trial in small cell lung cancer, a Phase 2 clinical trial in HIV-related Kaposi s sarcoma, a Phase 2 clinical trial in patients with late-stage glioblastoma (brain cancer), a Phase 1b clinical trial in combination with ifosfamide in patients with STS and a Phase 1b clinical trial in combination with gemcitabine in patients with metastatic solid tumors. We have completed a global Phase 2b clinical trial with aldoxorubicin as a 1st-line therapy for STS, a Phase 1b/2 clinical trial primarily in the same indication, a Phase 1b clinical trial 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 plan to expand our pipeline of oncology candidates through our drug-development activities at our laboratory facility in Freiburg, Germany, based on our Linker Activated Drug Release, or LADR , technology that can be utilized with multiple chemotherapeutic agents and may allow for greater drug concentration at tumor sites.

Table of Contents

***Our Product Candidate Pipeline***

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

| TECHNOLOGY | PRODUCT CANDIDATE | INDICATION | STAGE OF DEVELOPMENT |
|---|---|---|---|
| Doxorubicin conjugate | Aldoxorubicin | Soft Tissue Sarcoma | Global Pivotal Phase 3 ongoing<br>Global Phase 2b completed |
| | | Small-Cell Lung Cancer | Global Phase 2b ongoing |
| | | Glioblastoma Multiforme | Phase 2 ongoing |
| | | Kaposi s Sarcoma | Phase 2 ongoing |
| | | Combination with ifosfamide | Phase 1b ongoing |
| | | Combination with gemcitabine | Phase 1b ongoing |
| New albumin-binding drug conjugates | To be selected | To be selected | Pre-clinical |

***Our Clinical Development Programs***

Our current clinical development programs are discussed below.

*Aldoxorubicin*

Aldoxorubicin, a conjugate of the commonly prescribed chemotherapeutic agent doxorubicin, 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. In the first quarter of 2014, under an SPA agreed to by the FDA, we initiated a pivotal, global 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 increase the total doxorubicin dose, reduce several of the adverse events associated with native doxorubicin, achieve increased drug concentration at tumor sites and improve efficacy.

Our postulated mechanism of action for aldoxorubicin is as follows:

- after administration, aldoxorubicin rapidly forms a covalent bond to circulating albumin through an acid-sensitive 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

Table of Contents

- free doxorubicin is then released in the tumor.

*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, and its antitumor efficacy and its safety, including a reduction in cardiotoxicity. Animal studies conducted by aldoxorubicin inventor Dr. Felix Kratz, demonstrated statistically significant efficacy compared to both placebo and native doxorubicin against breast, ovarian, pancreatic and small cell lung cancers growing in immunodeficient mice.

We also previously announced additional data from a study of aldoxorubicin in immunodeficient mice transplanted with human glioblastoma cells in their brain, which showed that 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, published in the journal *Neoplasia* in October 2014, 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 slowing or reversing the progression 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, presented at the March 2006 Krebskongress meeting in Berlin, Germany, and published in the journal *Clinical Cancer Research* in August 2007. 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 10 of 13 (76.9%) evaluable patients with relapsed or refractory STS. The median number of aldoxorubicin cycles administered at the maximum tolerable dose was eight. The results of this clinical trial were published online in October 2014 in the journal *Cancer*.

In addition, best responses for the 13 evaluable STS trial subjects included the following: five (38.5%) achieved partial response (defined as shrinkage of target tumors by more than 30%); six (46%) showed prolonged stable disease (defined as tumor shrinkage by less than 30% from baseline or tumor growth less than 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, which is also observed with doxorubicin treatment, was resolved prior to the start of the next treatment. Final observed median PFS for advanced STS patients in the trial was 11.25 months, and median overall survival was 21.71 months. In addition, following eight cycles of aldoxorubicin, two patients experienced no progression of disease for 23 and 15 months, respectively, despite no further treatment.

Our Phase 1b pharmacokinetics clinical trial is 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. In connection with this trial, 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

approximately five minutes according to its package insert. Complete details from this Phase 1b clinical trial were published online in November 2014 in the journal *Investigational New Drugs*.

Table of Contents

We completed our global Phase 2b clinical trial to evaluate the preliminary efficacy and safety of aldoxorubicin as a 1st-line therapy in patients with advanced STS who are ineligible for surgery, which was initiated in December 2011. 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 1st-line therapy.

The Phase 2b clinical trial with aldoxorubicin in patients with STS was an international trial in 31 treatment centers under the direction of Sant 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 were to measure the PFS, tumor response and overall survival of patients with advanced STS treated with aldoxorubicin. This clinical trial also assessed 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/m2 of aldoxorubicin (83 subjects) or 75 mg/m2 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, overall survival and safety.

The central radiology review, as well as the investigators own assessments, showed an 80 107% improvement in PFS among patients treated with aldoxorubicin. In an intent-to-treat analysis, the investigator-assessed median PFS was 8.3 months for aldoxorubicin patients versus 4.6 months for doxorubicin patients (p=0.0006), while the blinded central radiology review indicated that median PFS for aldoxorubicin patients was 5.6 months versus 2.7 months for doxorubicin patients (p=0.0228). Per investigators, 68.1% of aldoxorubicin patients had not progressed at six months, compared with 33.0% of doxorubicin-treated patients (p=0.0005). As assessed by blinded central radiology review, 45.7% of aldoxorubicin patients had not progressed at six months, compared with 22.9% of doxorubicin patients (p=0.0195).

The overall response rate as determined by the investigators was 22.9% for aldoxorubicin subjects (2.4% complete response and 20.5% partial response) versus 5.0% for doxorubicin subjects (0% complete response and 5.0% partial response). As assessed by blinded central radiology review, 25.0% 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 investigators at study sites and by the blinded radiology review. The hazard ratio for investigator-read scans is 0.44 (95% confidence interval, range of 0.27 to 0.71) (p=0.0006), reflecting a 56% reduction in the risk of disease progression for patients treated with aldoxorubicin; and the hazard ratio for central lab scans is 0.60 (95% confidence interval, range of 0.38 to 0.95) (p=0.023), reflecting a 40% reduction in the risk of disease progression for the aldoxorubicin-treated patients. Hazard ratios are an important measure of the reliability and uniformity of the data for PFS, and when the upper limit is less than one, this indicates that there is a significant difference between the two study groups.

We also reported that a Kaplan-Meier analysis of the trial results which describes the duration of time for tumors to progress in individual patients, showed significant improvement in subjects treated with aldoxorubicin versus subjects treated with doxorubicin.

The overall survival results from the clinical trial demonstrated a 27% reduction in the risk of death compared to patients treated with doxorubicin (hazard ratio of 0.73: 95% confidence interval 0.44-1.20), the current standard-of-care in this indication. In addition, aldoxorubicin-treated patients demonstrated a 41% likelihood of surviving more than two years, a two-fold increase, compared to a 20% probability for doxorubicin-treated

patients. Median overall survival was 15.8 months (95% confidence interval 13.1-not reached) for aldoxorubicin-treated patients versus 14.3 months (95% confidence interval 8.7-20.9) for doxorubicin treated patients (p=0.21). For treatment-naive patients, representing 90% of the patients in the clinical trial, median

Table of Contents

overall survival was 15.8 months (95% confidence interval 13.1-not reached) for aldoxorubicin-treated patients versus 13.8 months (95% confidence interval 8.7-20.1) for doxorubicin treated patients (p=0.14).

In the Phase 2b clinical trial, aldoxorubicin was found to be relatively safe and well-tolerated. Subjects treated with aldoxorubicin had an approximately two-fold increase in severe neutropenia compared with doxorubicin-treated subjects, but there was no difference in the incidence of febrile neutropenia (indicating an infection may be present) between the two groups. All adverse events in subjects treated with aldoxorubicin were consistent with the known side effects of doxorubicin, and were usually resolved before 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, under an SPA agreed to by the FDA, we initiated a pivotal global Phase 3 clinical trial to evaluate the efficacy and safety of aldoxorubicin as a 2nd-line treatment for patients with STS. This multicenter, randomized, open-label Phase 3 clinical trial is designed to enroll approximately 400 patients with metastatic, locally advanced or unresectable STS, who have either not responded to or have progressed following treatment with, one or more systemic regimens of non-adjuvant chemotherapies. Trial patients will be randomized 1:1 to be treated with aldoxorubicin or the investigator s choice of an approved chemotherapeutic regimen, including doxorubicin, ifosfamide, dacarbazine, pazopanib (Votrient), or gemcitabine plus docetaxel, with up to three comparator regimens to be selected by the investigator at each clinical site. The primary endpoint of the study is PFS, and secondary endpoints include overall survival, response rates and safety. In January 2014, the Company announced it has received approval from the FDA to amend the Phase 3 protocol to continue dosing patients with aldoxorubicin until disease progression, which creates the potential for improved Phase 3 efficacy results.

Following discussions with the FDA, we reached agreement with the FDA on the design of the Phase 3 protocol under an SPA. As part of that assessment, the FDA agreed that the design and planned analysis of the study adequately addresses the objectives necessary to support a regulatory submission for approval.

The clinical trial is being conducted at approximately 85 clinical sites in the United States, Europe, Canada, Latin America, and Australia.

In September 2014, we initiated a global Phase 2b clinical trial evaluating aldoxorubicin compared to topotecan in subjects with extensive-stage small cell lung cancer, or SCLC, who have relapsed or were refractory to prior chemotherapy. The open-label Phase 2b clinical trial is expected to enroll approximately 132 patients (1:1 randomization). The primary endpoint is PFS and the secondary endpoints are overall survival, overall response rates (partial and complete) and the safety of aldoxorubicin compared to topotecan in this population. The study is expected to involve approximately 40 clinical trial sites in the United States, Spain, Italy and Hungary.

We are conducting 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 are conducting a Phase 2 clinical trial evaluating the preliminary efficacy of aldoxorubicin in patients with AIDS-related Kaposi s sarcoma, a tumor usually associated with HIV infection in the United States. 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 is expected to enroll up to 30 patients and is being conducted at the LSU Medical Center in New Orleans, Louisiana.

We are also conducting Phase 1b clinical trials of aldoxorubicin in combination with ifosfamide in subjects with STS, and in combination with gemcitabine in subjects with metastatic solid tumors. Since most

Table of Contents

chemotherapy agents are administered in combination with other chemotherapeutics, these studies will demonstrate the dose of aldoxorubicin that can be safely combined with two other chemotherapies that are commonly used to treated patients with sarcomas, pancreatic cancer, ovarian cancer and lung cancer.

*Drug Discovery Laboratory*

In October 2014, we commenced operations at our new discovery laboratory located in Freiburg, Germany. The laboratory is conducting discovery and translational research to create drug candidates which utilize our LADR technology and couple chemotherapeutic agents and proteins either inside the body or externally in order to concentrate the drug in tumors. Led by Felix Kratz, Ph.D., Vice President of Drug Discovery and inventor of aldoxorubicin, and Andre Warnecke, Ph.D., Senior Director of Drug Discovery, the discovery team is working to expand our novel albumin-binding anti-cancer drug pipeline using linkers that could also be used to create antibody-drug conjugates.

***Our Clinical Development Milestones***

The following table summarizes our current clinical development milestones:

| **2015** | **2016** | **2017** |
|---|---|---|
| þ 1H15: Preliminary Phase 2 GBM results expected | n 1Q16: Complete enrollment in Phase 3 STS trial | n 2017: NDA approval for aldoxorubicin in STS |
| þ 1H15: Preliminary results from Phase 2 Kaposi s sarcoma trial | n 1Q16: Complete enrollment in Phase 2b SCLC trial | n 2017: Commercial launch of aldoxorubicin for STS |
| þ 1H15: OS data expected from Phase 2b 1st-line STS trial | n 2H16: Phase 3 STS PFS data | |
| n 2H15: Report additional GBM and Kaposi s sarcoma clinical results | n 2H16: NDA filing in STS | |
| n 2H15: Complete enrollment in Phase 1s aldoxorubicin combination trials | n 2H16: Phase 2b 2nd-line SCLC data expected | |
| n 2H15: Select next drug-conjugate for clinical development | n 2016: Initiate Phase 1 trial with next drug-conjugate | |

These milestones are subject to the risks and uncertainties inherent in forward-looking statements and the other factors described in the Risk Factors section of this prospectus supplement, and our actual results may vary, perhaps dramatically, from our current estimates.

***Recent Developments***

In June 2015, we filed a provisional patent application in the United States that includes comprehensive claims directed to our LADR technology platform and related compositions of matter and methods.

On June 23, 2015, Cheryl Cohen was appointed to our board of directors. Ms. Cohen formerly served as the Chief Commercial Officer of Medivation, Inc., where she was responsible for the successful U.S. launch of Xtandi (enzalutamide) for metastatic castration-resistant prostate cancer.

***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 the prospectus.

Table of Contents

## 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 drug discovery activities and for general corporate purposes, which may include pre-commercialization activities relating to aldoxorubicin, working capital, capital expenditures, research and development and other commercial expenditures. See Use of Proceeds on page S-31 for further information. |
| Risk factors | See Risk Factors beginning on page S-12 of this prospectus supplement and page B-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 55,921,986 shares outstanding on March 31, 2015;
- assumes no exercise by the underwriters of their option to purchase up to an additional shares of our common stock;
- excludes 10,164,306 shares of our common stock subject to options outstanding as of March 31, 2015, having a weighted-average exercise price of $2.84 per share;
- excludes 539,034 shares of our common stock reserved for issuance under our stock option plans as of March 31, 2015; and
- excludes 7,292,617 shares of our common stock reserved for issuance upon exercise of outstanding warrants as of March 31, 2015, having a weighted-average exercise price of $4.29 per share.

Table of Contents

## 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 B-8 of the accompanying prospectus for additional risk factors.*

### Risks Associated With Our Business

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

We have operated at a loss due to our ongoing expenditures for research and development of our product candidates and for general and administrative purposes, and lack of significant recurring revenues. We incurred a net loss of $30.1 million and $17.5 million for the year ended December 31, 2014 and the three months ended March 31, 2015, respectively. We had an accumulated deficit as of March 31, 2015 of $324.0 million. We are likely to continue to incur losses unless and until we are able to commercialize aldoxorubicin or one or more future product candidates that we may develop or acquire. These losses, among other things, have had and will continue to have an adverse effect on our stockholders equity and working capital. We may never become profitable. If we become profitable, we may be unable to maintain our profitability, which could have a material adverse effect on the market value of our common stock.

***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 and proceeds from 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 fund development of product candidates based on our LADR technology;
- 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 candidate for which we obtain marketing approval and choose to market ourselves.

Our revenue was $0.1 million for the year ended December 31, 2014, and we realized no revenue in the three months ended March 31, 2015. We will have no significant recurring revenue unless we are able to commercialize aldoxorubicin, our lead product candidate, or one or more product candidates that we may develop or acquire, which commercialization may require us to first enter into license or other strategic arrangements with third parties.

At March 31, 2015, we had cash and cash equivalents of approximately $28.1 million and short-term investments of $37.1 million. Management believes that our current resources will be sufficient to fund our operations for the foreseeable future. The belief is based, in part, upon our currently projected expenditures for 2015 of approximately $56.3 million**,** which includes approximately $41.7 million for our clinical programs for aldoxorubicin, approximately $2.0 million for pre-clinical development of new albumin-binding cancer drugs, approximately $3.7 million for operation of our clinical programs and approximately $8.9 million for other general and administrative expenses. These projected expenditures are based upon numerous assumptions and subject to many uncertainties, and our actual expenditures may be significantly different from these projections.

Table of Contents

If we obtain marketing approval and successfully commercialize aldoxorubicin, or other product candidate, we anticipate it will take a minimum of two 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. 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, including the description in this prospectus supplement of our current drug development 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 estimated 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 estimates 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;

Table of Contents

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

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

- modification of the product during testing; and

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

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

Table of Contents

***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 2b clinical trial as a 1st-line treatment for STS; however, these conclusions may not be reproduced in future clinical trial results, including the ongoing Phase 3 clinical trial testing aldoxorubicin as a 2nd-line 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, or DSMB, 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. For example, the FDA placed a clinical hold on our clinical trials of aldoxorubicin in November 2014 following the death of an individual who was not enrolled in any of our clinical trials but who received aldoxorubicin pursuant to our compassionate use policy under a single-patient IND held by one of the clinical sites participating in our Phase 3 trial of aldoxorubicin in STS. The clinical hold resulted in our inability to enroll new

Table of Contents

patients in our aldoxorubicin studies until the hold was removed in February 2015. Although we have resumed enrollment in our studies, enrollment in our clinical trials and our projected development timelines may be adversely affected by residual effects of the former clinical hold or possible future clinical holds. For example, certain foreign regulatory authorities have not yet provided approval for enrollment to recommence in our Phase 3 trial of aldoxorubicin as a 2nd-line treatment for STS with the changes made to our protocol as a result of the clinical hold.

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 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. However, an SPA agreement does not guarantee approval of a product candidate, and even if the FDA agrees to the design, execution, and analysis proposed in protocols reviewed under the SPA process, the FDA may revoke or alter its agreement in certain circumstances. In particular, an SPA agreement is not binding on the FDA if public health concerns emerge that were unrecognized at the time of the SPA agreement, other new scientific concerns regarding product safety or efficacy arise, the sponsor fails to comply with the agreed upon trial protocols, or the relevant data, assumptions or information provided by the sponsor in a request for the SPA change or are found to be false or omit relevant facts. In addition, even after an SPA agreement is finalized, the SPA agreement may be modified, and such modification will be deemed binding on the FDA review division, except under the circumstances described above, if the FDA and the sponsor agree in writing to modify the protocol and such modification is intended to improve the study. The FDA retains significant latitude and discretion in interpreting the terms of the SPA agreement and the data and results from any study that is the subject of the SPA agreement. Moreover, 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.

Table of Contents

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

- if our product candidates receive marketing approval, the FDA could require us to adopt a Risk Evaluation and Mitigation Strategy to ensure that the benefits of any approved product candidate outweigh its risks;
- regulatory authorities may withdraw approvals of such product;
- regulatory authorities may require additional warnings on the label;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of aldoxorubicin or the particular product candidate at issue, if approved, and could significantly harm our business, results of operations and prospects.

***We rely on third parties to conduct our preclinical and clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we and our collaborators may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.***

We have agreements with third-party CROs to monitor and manage data for our preclinical and clinical programs. We rely heavily on these parties for execution of our preclinical and clinical trials, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on CROs does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with GCPs, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for products in clinical development. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of these CROs fails to comply with applicable GCP regulations, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, such regulatory authorities will determine that any of our clinical trials comply with the GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP regulations, and will require a large number of test subjects. Our or our CROs failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. In addition, our CROs are not our employees, and

except for remedies available to us under our agreements with such CROs, we cannot control whether or not they devote sufficient time and resources to our ongoing preclinical and clinical programs. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for aldoxorubicin would be harmed, our costs could increase and our ability to generate revenues could be delayed.

Switching or adding additional CROs involves substantial cost and requires extensive management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays can occur that can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these challenges or delays will not have a material adverse impact on our business, financial condition and prospects.

Table of Contents

***We rely upon third parties for the manufacture of our clinical product supplies, and we intend to rely on third parties to produce commercial supplies of any approved product candidate, and our commercialization of any product candidates, including aldoxorubicin, could be stopped, delayed or made less profitable if those third parties fail to obtain approval of the FDA, fail to provide us with sufficient quantities of drug product or fail to do so at acceptable quality levels or prices.***

We do not have the facilities or expertise to manufacture supplies of aldoxorubicin or any future product candidate, and we lack the resources and capability to manufacture product candidates on a clinical or commercial scale. 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 our current clinical programs for aldoxorubicin. However, we have no supply arrangements for the commercial manufacture of aldoxorubicin or manufacturing supply arrangements for any other product candidate, 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 product candidates or to commercialize them.

The facilities used by our contract manufacturers to manufacture our product candidates must be approved by the FDA pursuant to inspections that will be completed after we submit our new drug application, or NDA, to the FDA. We do not control the manufacturing process of aldoxorubicin and are completely dependent on our contract manufacturing partners for compliance with the FDA s requirements for manufacture of aldoxorubicin. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the FDA s strict regulatory requirements, they will not be able to secure or maintain FDA approval for the manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates.

If aldoxorubicin or any future product candidate 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 product candidate is approved for marketing cannot be manufactured at an acceptable cost, the commercial success of such product candidate may be adversely affected.

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

The marketing and commercialization of aldoxorubicin 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 aldoxorubicin, if it is approved for marketing.

Any future product candidate, 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 commercialize our products and may have to sell our rights in them to a third party or abandon their commercialization altogether.

To the extent we enter into collaborative arrangements, we will be dependent upon the timeliness and effectiveness of the development and marketing efforts of our contractual partners. If these companies do not allocate sufficient personnel and resources to these efforts or encounter difficulties in complying with applicable FDA and other

regulatory requirements, we may not obtain regulatory approvals as planned, if at all, and the timing of receipt or the amount of revenue from these arrangements may be materially and adversely affected. By entering into these arrangements, the potential profitability to us of these products may be less than if we were to complete the development and commercialization of these products on our own.

Table of Contents

***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 our LADR technology platform, these patents and applications may not prevent third parties from developing or commercializing similar or identical technologies. There is no assurance that any of our patent applications will issue, or that any of the patents will be enforceable or will cover a product or other commercially significant technology or method, or that the patents will be held to be valid for their expected terms.

The procedures for obtaining a patent in the United States and in most foreign countries are complex. These procedures require an analysis of sophisticated scientific and legal issues. Our patent position is very uncertain and we do not know when, or if, we will obtain additional patents for our products and technologies, or if the scope of the patents obtained will be sufficient to protect our products and technologies, or be considered sufficient by parties reviewing our patent positions pursuant to a potential marketing, licensing or financing transaction.

In addition, other entities may challenge the validity or enforceability of our patents and patent applications in litigation or administrative proceedings. Even the issuance of a patent is not conclusive as to its validity or enforceability. We cannot make assurances as to how much protection, if any, will be given to our patents if we attempt to enforce them or they are challenged. It is possible that a competitor or a generic pharmaceutical provider may successfully challenge our patents and those challenges may result in reduction or elimination of our patents coverage.

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 and pharmaceutical 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 technologies, or discourage our existing licensees from continuing their development work on our potential products or technologies. If our patent coverage is insufficient to prevent third parties from developing or commercializing similar or identical products or 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 or technologies 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. There exists numerous U.S. and foreign issued patents and pending patent applications owned by others, including our licensor KTB Tumorforschungs GmbH, that relate to aldoxorubicin. Numerous U.S. and foreign issued patents and pending patent applications owned by others also exist in the therapeutic areas in which we are developing products. There are also numerous issued patents and patent

Table of Contents

applications to chemical compounds or synthetic processes that may be necessary or useful to use in our research, development, manufacturing or commercialization activities. These could materially affect our ability to develop our products or technologies or manufacture, import or sell products, and our activities, or those of our licensors or collaborators, could be determined to infringe these patents. Moreover, we may not know about patents or patent applications that our products or technologies might 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 or technologies might 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 or derivation proceedings in the U.S. Patent and Trademark Office to determine priority of invention. If third parties file post grant challenges (such as Post Grant Review (PGR), Inter Partes Review (IPR) and Ex Parte Reexamination) in the U.S., we may have to participate in defending the patentability of our U.S. patents in the U.S. Patent and Trademark Office. 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 patents or patent applications.

If a third party claims that we infringe its proprietary rights:

- 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 product or technology infringes a competitor s patent;
- a court may prohibit us from selling or licensing our product or technology without a license from the patent holder, which may not be available on commercially acceptable terms, if at all, or which may require us to pay substantial royalties or grant cross licenses to our patents; and
- we may have to redesign our product candidates or technology so that it does not infringe patent rights of others, which may not be possible or commercially feasible.

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

***Any products we develop may become subject to unfavorable pricing regulations or third-party coverage and reimbursement policies, which could have a material adverse effect on our business.***

We currently intend to sell our products that may be approved for marketing primarily to hospitals, which generally 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.

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.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, third-party payors, including private and governmental payor, such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs will be covered and reimbursed. The Medicare program covers certain individuals aged 65 or older, disabled or suffering from end-stage renal disease. The Medicaid program, which varies from state-to-state, covers certain individuals and families who have limited financial means. The Medicare and Medicaid programs increasingly are used as models for how private payors and other governmental payors develop their coverage and reimbursement policies for drugs and biologics. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates.

Table of Contents

Most third-party payors may deny coverage or 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 cover and 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, third-party payors 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.

***Healthcare legislative reform measures could hinder or prevent the commercial success of our products and product candidates.***

In the United States, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system that could affect our future revenues and profitability. Federal and state lawmakers regularly propose and, at times, enact legislation that results in significant changes to the healthcare system, some of which are intended to contain or reduce the costs of medical products and services. For example, in March 2010, President Obama signed one of the most significant healthcare reform measures in decades, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the Affordable Care Act. It contains a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement changes and fraud and abuse measures, all of which will impact existing government healthcare programs and will result in the development of new programs. The Affordable Care Act, among other things: (i) increases the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program, extends the rebate program to individuals enrolled in Medicaid managed care organizations, and addresses new methodologies by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, and for drugs that are line extension products; (ii) establishes annual fees and taxes on manufacturers of certain branded prescription drugs: and (iii) enacts a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer s outpatient drugs to be covered under Medicare Part D.

In addition, other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. On August 2, 2011, the Budget Control Act of 2011 among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation s automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments, will remain in effect through 2024 unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our products once approved or additional pricing pressures.

***We may also be subject to healthcare laws, regulation and enforcement and our failure to comply with those laws could adversely affect our business, operations and financial condition.***

If we obtain FDA approval for any of our product candidates and begin commercializing those products in the United States, our operations may be directly, or indirectly through our customers, subject to various federal and state fraud

and abuse laws, including, without limitation, the federal Anti-Kickback Statute, the federal False Claims Act, and physician sunshine laws and regulations. These laws may impact, among other things, our proposed sales, marketing, and education programs. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which prohibits, among other things, any person from knowingly and willfully offering, soliciting, receiving or providing remuneration, directly or indirectly, to induce either the

Table of Contents

referral of an individual, for an item or service or the purchasing or ordering of a good or service, for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs;

- the federal False Claims Act, which prohibits, among other things, individuals or entities from knowingly presenting, or causing to be presented, false claims, or knowingly using false statements, to obtain payment from the federal government, and which may apply to entities that provide coding and billing advice to customers;

- federal criminal laws that prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

- the federal physician sunshine requirements under the Affordable Care Act, which requires manufacturers of drugs, devices, biologics, and medical supplies to report annually to the Centers for Medicare & Medicaid Services information related to payments and other transfers of value to physicians, other healthcare providers, and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members;

- the federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, which governs the conduct of certain electronic healthcare transactions and protects the security and privacy of protected health information; and

- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry s voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. In addition, recent health care reform legislation has strengthened these laws. For example, the recently enacted Affordable Care Act, among other things, amends the intent requirement of the Federal Anti-Kickback Statute and criminal healthcare fraud statutes. A person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it. In addition, the Affordable Care Act provides that the government may assert that a claim including items or services resulting from a violation of the Federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

Achieving and sustaining compliance with these laws may prove costly. In addition, any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management s attention from the operation of our business. If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties,

including civil and criminal penalties, damages, fines, the exclusion from participation in federal and state healthcare programs, imprisonment, or the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our financial results.

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

Aldoxorubicin is a conjugate of doxorubicin, a widely used anti-cancer drug. Doxorubicin is part of the anthracycline class of chemotherapy agents. Anthracyclines, many of which, including doxorubicin are generic, have been used throughout the world to treat various cancers for several decades. Due to their track record of broad anti-cancer activity, new types of anthracyclines and modified or reformulated versions continue to be developed to overcome toxicities which limit the use of these drugs.

Aldoxorubicin is a chemically modified version of doxorubicin that incorporates an acid sensitive linker technology to improve concentration in the tumor. We believe that the albumin-binding ability of aldoxorubicin will allow the compound to overcome many of the side effect issues typically associated with anthracyclines. We also believe that using albumin as a targeted carrier will allow for higher dosing, greater concentration of the drug in tumors and greater efficacy.

Table of Contents

STS patients are typically treated with surgery followed by radiation therapy. For patients ineligible for surgery, radiation or chemotherapy, or both, is the only option. Doxorubicin is the only approved first-line drug for treating STS 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, gemcitabine with docetaxel, dacarbazine and liposomal doxorubicin marketed in the United States as Doxil® by Johnson & Johnson. GlaxoSmithKline s pazopanib (Votrient®) was approved in the United States and Europe in 2012 for the treatment of certain types of advanced STS following prior chemotherapy. There are other approaches to treating STS in clinical development, including Threshold Pharmaceuticals TH-302 currently in a Phase 3 clinical trial and Tracon Pharmaceuticals TRC-105 in combination with pazopanib. In November 2014, the Janssen unit of Johnson & Johnson submitted an NDA to the FDA for trabectedin (Yondelis®) for the treatment of patients with advanced STS, including leiomyosarcoma and liposarcoma, that have previously received an anthracycline and ifosfamide or an anthracycline followed by another chemotherapy. The FDA granted a priority review for the trabectedin NDA in February 2015. Trabectedin is being co-developed by Johnson & Johnson and PharmaMar. In February 2015, Eisai announced that eribulin (Halaven®) met the primary endpoint of overall survival in patients with either adipocytic or leiomyosarcoma following prior treatment with an anthracycline and at least one additional regimen.

Patients with glioblastoma multiforme, or GBM, generally undergo invasive brain surgery, although disease progression following surgery is nearly 100%. The front-line therapy for GBM following surgery is radiation in combination with temozolomide (Temodar®). Bevacizumab (Avastin®) has been approved for the treatment of GBM in patients progressing after prior therapy. Drugs in development to treat GBM include rindopepimut by Celldex Therapeutics, nivolumab by Bristol-Myers Squibb, DCVax by Northwest Biotherapeutics, TRC105 from Tracon Pharmaceuticals, veliparib by AstraZeneca and buparlisib by Novartis.

Treatment for newly diagnosed SCLC, typically consists of cisplatin or carboplatin in combination with etoposide. Radiation may also be given for extensive-stage disease. While first-line treatment can yield overall response rates of 50%-80%, the duration of response is often less than 90 days. For recurrent SCLC, topotecan (Hycamtin®) is standard therapy. SCLC patients who are sensitive to first-line treatment may receive topotecan or the generic chemotherapeutic drugs irinotecan, taxanes, gemcitabine or vinorelbine. Drugs in development for second-line SCLC include Bristol-Myers Squibb s ipilumimab (Yervoy®) and SC16LD6.5 by Stem CentRx, Inc.

Kaposi s sarcoma is generally treated with radiation, surgery or liposomal doxorubicin, or both. Liposomal daunorubicin (DaunoXome®, Galen US), with or without paclitaxel, is also recommended as treatment for advanced Kaposi s sarcoma. 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.

As a result, these competitors may:

- succeed in developing competitive products sooner than us or our strategic partners or licensees;
- obtain FDA or foreign governmental approvals for their products before we can obtain approval of any of our products;

Table of Contents

- obtain patents that block or otherwise inhibit the development and commercialization of our product candidate candidates;
- develop products that are safer or more effective than our products;
- devote greater resources than us to marketing or selling products;
- introduce or adapt more quickly than us to new technologies and other scientific advances;
- introduce products that render our products obsolete;
- withstand price competition more successfully than us or our strategic partners or licensees;
- negotiate third-party strategic alliances or licensing arrangements more effectively than us; and
- take better advantage than us of other opportunities.

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

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

- commercially reasonable royalties based on a percentage of net sales (as defined in the agreement);
- a percentage of any non-royalty sub-licensing income (as defined in the agreement); and
- milestones of $1,000,000 for each additional final marketing approval that we obtain.

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

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

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

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

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

- foreign regulatory requirements that could restrict or limit our ability to conduct our clinical trials;
- administrative burdens of conducting clinical trials under multiple foreign regulatory schema;
- foreign exchange fluctuations;
- diminished protection of intellectual property in some countries; and
- possible nationalization and expropriation.

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

Table of Contents

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

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

***Drug discovery is a complex, time-consuming and expensive process, and we may not succeed in creating new product candidates.***

Conducting drug discovery and pre-clinical development of our albumin-binding technology is a complex and expensive process that will take many years. Accordingly, we cannot be sure whether or when our drug discovery and pre-clinical development activities will succeed in developing any new product candidates. In addition, any product candidates that we develop in pre-clinical testing may not demonstrate success in clinical trials required for marketing approval.

Any deficiency in the design, implementation or oversight of our drug discovery and pre-clinical testing programs could cause us to incur significant additional costs, experience significant delays, prevent us from obtaining marketing approval for any product candidate that may result from these programs or abandon development of certain product candidates. If any of these risks materializes, it could harm our business and cause our stock price to decline.

***We have a limited operating history in drug discovery, which is inherently risky, and we may not succeed in addressing these risks.***

We have operated our drug discovery laboratory in Freiberg, Germany, and LADR development program only since October 2014. Accordingly, we have a limited operating history in conducting our own drug discovery programs. We have not yet demonstrated the ability to successfully create new product candidates. Consequently, there is limited information for investors to use as basis for assessing the viability of our drug discovery efforts based on our LADR technology. Investors must consider the risks and difficulties inherent in drug discovery and pre-clinical activities, including the following:

- difficulties, complications, delays and other unanticipated factors in connection with the development of new drugs;
- competition from companies that have substantially greater assets and financial resources than we have;
- our ability to anticipate and adapt to a competitive market and rapid technological developments;
- our need to rely on multiple levels of complex financing agreements with outside funding due to the length of drug development cycles and governmental approved protocols associated with the pharmaceutical industry; and

- our dependence upon key scientific personnel, including Felix Kratz, Ph.D., our Vice President of Drug Discovery, and Andre Warnecke, Ph.D., our Senior Director of Drug Discovery.

We cannot be certain that we will successfully address these risks or that our drug discovery efforts will be successful. In the event that we do not successfully address these risks, our business, prospects, financial condition and results of operations could be materially and adversely affected. We also may be required to reduce or discontinue altogether our drug discovery and pre-clinical programs.

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

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

Table of Contents

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

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

***Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.***

Under Section 382 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an ownership change, the corporation s ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes (such as research and development tax credits) to offset its post-change income and taxes may be limited. In general, an ownership change occurs if there is a cumulative change in our ownership by 5% shareholders that exceeds 50 percentage points over a rolling three-year period. Similar rules may apply under state tax laws. As a result of a previous ownership change, our annual utilization of approximately $62.3 million in federal net operating loss carryforwards will be substantially limited. If we experience one or more ownership changes as a result of this offering or future transactions in our stock, we may be further limited in our ability to use our net operating loss carryforwards and other tax assets. Any such limitations on the ability to use our net operating loss carryforwards and other tax assets could potentially result in increased future tax liability to us on any net income that we may earn in the future.

**Risks Associated With This Offering And Our Common Stock**

***Our management will have broad discretion as to the use of the proceeds of this offering.***

We have not designated the amount of net proceeds we will receive from this offering for any particular purpose. Accordingly, our management will have broad discretion as to the application of these net proceeds and could use them for purposes other than those contemplated at the time of this offering. Our stockholders may not agree with the manner in which our management chooses to allocate and spend the net proceeds.

***You will experience immediate and substantial dilution in the net tangible book value per share of the stock you purchase.***

Since the price per share of our common stock being offered is higher than the net tangible book value per share of our common stock, you will suffer substantial dilution in the net tangible book value of the common stock you purchase in this offering. Based on the public offering price of $ per share, and after deducting the underwriting discounts and commissions and the estimated offering expenses payable by us, if you purchase shares of common stock in this offering, you will suffer immediate and substantial dilution of $ per share in the net tangible book value of the common stock. See Dilution in this prospectus supplement for a more detailed discussion of the dilution you will incur if you purchase common stock in this offering.

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

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

paid by investors in this offering. The price per share at which we sell additional shares of our common stock or other securities convertible into or exchangeable for our common stock in future transactions may be higher or lower than the price per share in this offering.

***We may experience volatility in our stock price, which may adversely affect the trading price of our common stock.***

The market price of our common stock has ranged from a low of $2.51 to a high of $5.42 per share during the period January 1, 2015 through July 17, 2015, and it may continue to experience significant volatility from time to time. Factors that may affect the market price of our common stock include the following:

- announcements of interim or final results of our clinical trials or our drug discovery activities;
- announcements of regulatory developments or technological innovations by us or our competitors;
- changes in our relationship with our licensors and other strategic partners;

Table of Contents

- our quarterly operating results;
- litigation involving or affecting us;
- shortfalls in our actual financial results compared to our guidance or the forecasts of stock market analysts;
- developments in patent or other technology ownership rights;
- acquisitions or strategic alliances by us or our competitors;
- public concern regarding the safety of our products; and
- government regulation of drug pricing.

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

As of March 31,2015, we had outstanding stock options to purchase 10,164,306 shares of our common stock at a weighted-average exercise price of $2.84 per share and outstanding warrants to purchase 7,292,617 shares of common stock at a weighted-average exercise price of $4.29 per share. At the annual meeting of stockholders held on June 23, 2015, our stockholders approved an amendment to our 2008 Stock Incentive Plan to increase the number of shares of our common stock available for issuance under the Plan by 10,000,000 shares. Our outstanding options and warrants and any options and warrants that we may grant or issue in the future could adversely affect our ability to obtain future financing or engage in certain mergers or other transactions, since the holders of options and warrants can be expected to exercise them at a time when we may be able to obtain additional capital through a new offering of securities on terms more favorable to us than the terms of outstanding options and warrants. For the life of the options and warrants, the holders have the opportunity to profit from a rise in the market price of our common stock without assuming the risk of ownership. The issuance of shares upon the exercise of outstanding options and warrants will also dilute the ownership interests of our existing stockholders.

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

***We are subject to pending legal claims that could adversely affect our financial condition and results of operations and our business or result in changes in our corporate governance. We recently entered into a settlement of a stockholder derivative lawsuit against a number of our current and former directors and officers that is subject to Court approval.***

On June 13, 2014, three purported securities class action lawsuits pending against us and certain of our officers and directors in the United States District Court for the Central District of California were consolidated in the matter of *In re CytRx Corporation Securities Litigation*, 2:14-CV-01956-GHK (PJWx), and lead plaintiff and lead counsel were appointed. On October 1, 2014, plaintiffs filed a consolidated amended complaint on behalf of all persons who

purchased or otherwise acquired our publicly traded securities between November 20, 2013 and March 13, 2014, against us, certain of our officers and directors, a freelance writer, and certain underwriters, including Jefferies LLC, Oppenheimer & Co., LLC, Aegis Corp., and H.C. Wainwright & Co., LLC. The complaint alleges that certain of the defendants violated the Securities Exchange Act of 1934 by making materially false and misleading statements in press releases, promotional articles, SEC filings and other public statements. The complaint further alleges that certain of the defendants violated the Securities Act of 1933 by making materially misleading statements and omitting material information in our shelf Registration Statement on Form S-3 filed with the SEC on December 6, 2012 and Prospectus Supplement under Rule 424(b)(2) filed with the SEC on January 31, 2014. These allegations arise out of our alleged retention of The DreamTeam Group and MissionIR, external investor and public relations firms unaffiliated with us, as well as our December 9, 2013 grant of stock options to certain board members and officers. The consolidated amended complaint seeks damages, including interest, in an unspecified amount, reasonable costs and attorneys fees, and any equitable, injunctive, or other relief that the court may deem just and proper. On December 5, 2014, we and the individual defendants filed a motion to dismiss the complaint. The Court was scheduled to hear argument on this motion on March 2, 2015. On February 25, 2015, the Court took this motion under submission and took the hearing off calendar. On July 13, 2015, the Court issued an order granting in part and denying in part the motions to dismiss filed by us, the individual defendants and the underwriters. The Court afforded the plaintiffs 30 days to amend their complaint, if they elect to do so.

On April 3, 2014, a purported class action lawsuit was filed against us and certain of our officers and each of our directors, as well as certain underwriters, in the Superior Court of California, County of Los Angeles, captioned

Table of Contents

*Rajasekaran v. CytRx Corporation, et al.*, BC541426. The complaint purports to be brought on behalf of all shareholders who purchased or otherwise acquired our common stock pursuant or traceable to our public offering that closed on February 5, 2014. The complaint alleges that defendants violated the federal securities laws by making materially false and misleading statements in our filings with the SEC. The complaint seeks compensatory damages in an unspecified amount, rescission, and attorney s fees and costs. On October 14, 2014, the Court granted the parties joint ex parte motion to stay this proceeding pending resolution of motions to dismiss in the related federal action, *In re CytRx Corporation Securities Litigation*, 2:14-CV-01956-GHK (PJWx).

On July 3, 2014, a shareholder derivative lawsuit was filed in the United States District Court for the Central District of California, captioned *Fishman v. Kriegsman, et al.*, 2:14-cv-05169, purportedly on our behalf against certain of our officers and each of our directors. The complaint alleges breach of fiduciary duties, corporate waste, gross mismanagement, and unjust enrichment in connection with our alleged retention of DreamTeamGroup and MissionIR. The complaint seeks damages, restitution, corporate governance reforms, and attorney s fees and costs. On September 3, 2014, plaintiff filed a notice to voluntarily dismiss this action against all parties without prejudice, which the Court granted on September 9, 2014.

On September 10, 2014, the Delaware Court of Chancery consolidated *Schwartz v. Ignarro, et al.*, Case No. 9864, *Johnson v. Ignarro, et al.*, Case No. 9884, and *Silverberg v. Kriegsman, et al.*, Case No. 9919, three shareholder derivative lawsuits described in our Quarterly Report filed with the SEC on August 6, 2014. The allegations in the *Schwartz* and *Johnson* complaints relate to our December 9, 2013 grant of stock options to certain board members and officers. The allegations in the *Silverberg* complaint relate to our December 9, 2013 grant of stock options to certain board members and officers, as well as our alleged retention of DreamTeamGroup and MissionIR. A consolidated complaint concentrated on the stock-option grant claims was filed on October 9, 2014. The consolidated lawsuit is captioned *In re CytRx Corp. Stockholder Derivative Litigation,* C.A. No. 9864-VCL. On November 10, 2014, we and the individual defendants filed a motion to dismiss the consolidated complaint or, in the alternative, to stay the action. The Court heard argument on the motions on January 8, 2015. The Court denied the motion to dismiss and granted in part and denied in part the motion to stay.

On June 2, 2015, we announced that we had reached an agreement to settle the Delaware stockholder derivative action. Under the settlement, we have agreed to re-price stock options to purchase a total of 2,095,000 shares of our common stock that were granted on December 10, 2013 to certain of our directors and officers from the original exercise price of $2.39 to an exercise price of $4.66 (the share price at market closing on December 20, 2013). The settlement also provides that we will implement certain corporate governance changes and modify our governance practices regarding the granting of stock options. The parties have not yet reached an agreement on an amount of any award of fees and expenses to plaintiffs attorneys, which award must be approved by the Court regardless of whether there is an agreement between the parties. The settlement is subject to the drafting of definitive documentation, notice to stockholders, and Court approval.

On August 14, 2014, a shareholder derivative lawsuit, captioned *Pankratz v. Kriegsman, et al.*, 2:14-cv-06414-PA-JPR, was filed in the United States District Court for the Central District of California purportedly on our behalf against certain of our officers and each of our directors. The complaint alleges breach of fiduciary duties, unjust enrichment, gross mismanagement, abuse of control, insider selling and misappropriation of information in connection with our alleged retention of DreamTeamGroup and MissionIR, as well as our December 9, 2013 grant of stock options to certain board members and officers. The complaint seeks unspecified damages, corporate governance and internal procedures reforms, restitution, disgorgement of all profits, benefits, and other compensation obtained by the individual defendants, and the costs and disbursements of the action.

On August 15, 2014, a shareholder derivative complaint, captioned *Taylor v. Kriegsman, et al.*, 2:14-cv-06451, was filed in the United States District Court for the Central District of California purportedly on our behalf against certain of our officers and each of our directors. The complaint alleges breach of fiduciary duties, unjust enrichment, gross mismanagement, abuse of control, unjust enrichment, insider selling and misappropriation of information in connection with our alleged retention of DreamTeamGroup and MissionIR, as well as our December 9, 2013 grant of stock options to certain board members and officers. The complaint seeks unspecified damages, corporate governance and internal procedures reforms, restitution, disgorgement of all profits, benefits, and other compensation obtained by the individual defendants, and the costs and disbursements of the action.

Table of Contents

On October 8, 2014, the Court in *Pankratz* and *Taylor* consolidated the cases and appointed lead plaintiffs and co-lead counsel. On October 20, 2014, we and the individual defendants filed motions to dismiss the consolidated *Pankratz* and *Taylor* cases or, in the alternative, to stay the cases. On January 9, 2015, the Court stayed the action pending the resolution of the consolidated Delaware derivative action. On February 27, 2015, the *Pankratz* and *Taylor* plaintiffs filed a motion to vacate the stay. On June 24, 2015, the Court granted the motion to lift the stay in light of the pending settlement of the Delaware derivative litigation discussed above. The Court further denied the motion to dismiss without prejudice and invited us to move to dismiss the case within 30 days pursuant to the doctrine of *forum non conveniens* based on our forum-selection bylaw, which mandates that derivative actions be filed in Delaware. The Court advised that it would consider any *forum non conveniens* motion before considering a subsequent motion to dismiss under Rule 12.

Adverse outcomes with respect to some or all of the foregoing claims may result in an award of monetary damages against us that could exceed our available insurance coverage and that could have a material adverse effect on our working capital and results of operations. These claims also may divert the time and attention of our management and harm our business or result in changes in the composition of our board of directors or other corporate governance that we cannot predict. These claims are subject to inherent uncertainties, and management s view of these matters may change in the future. If an unfavorable outcome becomes probable and reasonably estimable, we could incur charges that could have a material adverse impact on our financial condition and results of operations for the period in which the outcome becomes probably and reasonably estimable.

***Our anti-takeover measures may make it more difficult to change our management, or may discourage others from acquiring us, and thereby adversely affect stockholder value.***

We have a stockholder rights plan and provisions in our restated by-laws, as amended, that are intended to protect our stockholders interests by encouraging anyone seeking control of our company to negotiate with our board of directors. These provisions may discourage or prevent a person or group from acquiring us without the approval of our board of directors, even if the acquisition would be beneficial to our stockholders.

We have a classified board of directors, which means that at least two stockholder meetings, instead of one, will be required to effect a change in the majority control of our board of directors. This applies to every election of directors, not just an election occurring after a change in control. The classification of our board increases the amount of time it takes to change majority control of our board of directors and may cause potential acquirers to lose interest in a potential purchase of us, regardless of whether our purchase would be beneficial to us or our stockholders. The additional time and cost to change a majority of the members of our board of directors makes it more difficult and may discourage our existing stockholders from seeking to change our existing management in order to change the strategic direction or operational performance of our company.

Our by-laws provide that directors may only be removed for cause by the affirmative vote of the holders of at least a majority of the outstanding shares of our capital stock then entitled to vote at an election of directors. This provision prevents stockholders from removing any incumbent director without cause. Our by-laws also provide that a stockholder must give us at least 120 days notice of a proposal or director nomination that such stockholder desires to present at any annual meeting or special meeting of stockholders. Such provision prevents a stockholder from making a proposal or director nomination at a stockholder meeting without us having advance notice of that proposal or director nomination. This could make a change in control more difficult by providing our directors with more time to prepare an opposition to a proposed change in control. By making it more difficult to remove or install new directors, these by-law provisions may also make our existing management less responsive to the views of our stockholders with respect to our operations and other issues such as management selection and management compensation.

We are subject to the anti-takeover provisions of Section 203 of the Delaware General Corporation Law, which may also prevent or delay a takeover of us that may be beneficial to our stockholders.

Table of Contents

***Our restated by-laws, as amended, designate the Court of Chancery of the State of Delaware as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders ability to obtain a favorable judicial forum for disputes with us or our directors, officers or other employees.***

Our restated by-laws, as amended, provide that, unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any director, officer or other employee to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, or (iv) any action asserting a claim that is governed by the internal affairs doctrine. Any person purchasing or otherwise acquiring any interest in any shares of our capital stock shall be deemed to have notice of and to have consented to this provision of our by-laws. This choice-of-forum provision may limit our stockholders ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits. Alternatively, if a court were to find this provision of our by-laws inapplicable or unenforceable with respect to one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could adversely affect our business and financial condition.

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

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

***We do not expect to pay any cash dividends on our common stock.***

We have not declared or paid any cash dividends on our common stock or other securities, and we currently do not anticipate paying any cash dividends in the foreseeable future. Because we do not anticipate paying cash dividends for the foreseeable future, our stockholders will not realize a return on their investment in our common stock except to the extent of any appreciation in the value of our common stock. Our common stock may not appreciate in value, or may decline in value.

Table of Contents

## USE OF PROCEEDS

We estimate that the net proceeds of this offering, after deducting the underwriting discounts and commissions and the estimated offering expenses payable by us, will be approximately $ million (or approximately $ million if the underwriters exercise their option to purchase additional shares of common stock in full).

We intend to use the net proceeds of this offering to fund our clinical trials of aldoxorubicin and our drug discovery activities and for general corporate purposes, which may include pre-commercialization activities relating to Aldoxorubicin, working capital, capital expenditures, research and development and other commercial expenditures. We also may use a portion of the net proceeds to acquire additional product candidates or complementary assets or businesses, although we have no understandings or commitments to do so. As of the date of this prospectus supplement, we cannot specify with certainty the particular uses of the proceeds from this offering. As a result, our management will retain broad discretion in the allocation and use of the net proceeds from this offering. Pending their use as described above, we intend to invest the net proceeds of this offering in high-quality, short-term, interest-bearing securities.

Table of Contents

## DIVIDEND POLICY

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

Table of Contents

## CAPITALIZATION

The following table sets forth our cash and cash equivalents and capitalization as of March 31, 2015:

- on an actual basis; and
- on an as adjusted basis to give effect to the issuance of shares of our common stock, at the public offering price of $ per share, after deducting the underwriting discounts and commissions and the estimated offering expenses payable by us, assuming no exercise of the underwriters option to purchase additional shares.

The information set forth in the following table should be read in conjunction with and is qualified in its entirety by our Management s Discussion and Analysis of Financial Condition and Results of Operations and consolidated financial statements and notes thereto incorporated by reference in this prospectus supplement and the accompanying prospectus. See Summary The Offering in this prospectus supplement for information relating to the expected number of shares of our common stock to be outstanding after this offering.

| | AS OF MARCH 31, 2015 | |
|---|---|---|
| **(unaudited) (in thousands, except share data)** | **ACTUAL** | **AS ADJUSTED** |
| Cash and cash equivalents | $ 28,053 | $ |
| Short-term investments | 37,102 | |
| Total assets | 73,766 | |
| Stockholders equity: | | |
| Preferred Stock, $0.01 par value, 5,000,000 shares authorized, including 25,000 authorized shares of Series A Junior Participating Preferred Stock; no shares issued and outstanding | | |
| Common stock: $0.001 par value; 250,000,000 shares authorized; 55,921,986 shares issued and outstanding, actual; shares issued and outstanding, as adjusted | 56 | |
| Additional paid-in capital | 378,361 | |
| Treasury stock, at cost (199,275 shares) | (2,613) | (2,613) |
| Accumulated deficit | (324,032) | (324,032) |
| Total stockholders equity | 51,772 | |
| Total liabilities and stockholders equity | $ 73,766 | $ |

Table of Contents

## DILUTION

Purchasers of common stock offered by this prospectus supplement and the accompanying prospectus will suffer immediate and substantial dilution in the net tangible book value per share of common stock. Our net tangible book value as of March 31, 2015 was approximately $ per share of our common stock. Net tangible book value per share represents the amount of total tangible assets less total liabilities, divided by the number of shares of our common stock outstanding as of March 31, 2015.

Dilution in net tangible book value per share represents the difference between the amount per share paid by purchasers in this offering and the net tangible book value per share of our common stock immediately after this offering. After giving effect to the sale of shares of common stock in this offering at a public offering price of $ per share, and after deducting the underwriting discounts and commissions and the estimated offering expenses payable by us, our as adjusted net tangible book value as of March 31, 2015 would have been approximately $ per share of our common stock. This represents an immediate increase in net tangible book value of $ per share of our common stock to our existing stockholders and an immediate dilution in net tangible book value of $ per share of our common stock to investors participating in this offering. The following table illustrates this per share dilution:

| | | |
|---|---|---|
| Public offering price per share | | $ |
| Net tangible book value per share as of March 31, 2015 | $ | |
| Increase per share attributable to this offering | $ | |
| As adjusted net tangible book value per share as of March 31, 2015 after this offering | | $ |
| Dilution per share to new investors participating in this offering | | $ |

The above table is based on 55,921,986 shares of common stock outstanding as of March 31, 2015, and excludes:

- 10,164,306 shares of our common stock subject to options outstanding as of March 31, 2015, having a weighted-average exercise price of $2.84 per share;
- 539,034 shares of our common stock reserved for issuance in connection with future grants under our stock option plans as of March 31, 2015; and
- 7,292,617 shares of our common stock reserved for issuance upon exercise of outstanding warrants as of March 31, 2015, having a weighted-average exercise price of $4.29 per share.

If the underwriters exercise in full their option to purchase shares of common stock at the public offering price of $ share, less the underwriting discounts and commissions, the as adjusted net tangible book value after this offering would be $ share, representing an increase in net tangible book value of $ share to existing stockholders and immediate dilution in net tangible book value of $ per share to purchasers in this offering at the public offering price.

To the extent that any options or warrants are exercised, new options are issued under our equity incentive plans or we otherwise issue additional shares of common stock in the future at a price less than the public offering price, there may be further dilution to purchasers of common stock in this offering.

Table of Contents

## MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES TO NON-U.S. HOLDERS OF OUR COMMON STOCK

The following discussion is a summary of the material U.S. federal income tax consequences to non-U.S. holders (as defined below) of the purchase, ownership and disposition of our common stock issued pursuant to this offering, but does not purport to be a complete analysis of all potential tax effects. The effects of other U.S. federal tax laws, such as estate and gift tax laws, and any applicable state, local or foreign tax laws are not discussed. This discussion is based on the Internal Revenue Code of 1986, as amended, or the Code, Treasury Regulations promulgated thereunder, judicial decisions, and published rulings and administrative pronouncements of the U.S. Internal Revenue Service, or IRS, in effect as of the date of this offering. These authorities may change or be subject to differing interpretations. Any such change may be applied retroactively in a manner that could adversely affect a non-U.S. holder of our common stock. We have not sought and will not seek any rulings from the IRS regarding the matters discussed below. There can be no assurance the IRS or a court will not take a contrary position regarding the tax consequences of the purchase, ownership and disposition of our common stock.

This discussion is limited to non-U.S. holders that hold our common stock as a capital asset within the meaning of Section 1221 of the Code (property held for investment). This discussion does not address all U.S. federal income tax consequences relevant to a non-U.S. holder s particular circumstances, including the impact of the unearned income Medicare contribution tax. In addition, it does not address consequences relevant to non-U.S. holders subject to particular rules, including, without limitation:

- U.S. expatriates and certain former citizens or long-term residents of the United States;
- persons subject to the alternative minimum tax;
- persons holding our common stock as part of a hedge, straddle or other risk reduction strategy or as part of a conversion transaction or other integrated investment;
- banks, insurance companies, and other financial institutions;
- brokers, dealers or traders in securities;
- controlled foreign corporations, passive foreign investment companies, and corporations that accumulate earnings to avoid U.S. federal income tax;
- partnerships or other entities or arrangements treated as partnerships for U.S. federal income tax purposes;
- tax-exempt organizations or governmental organizations;

- persons deemed to sell our common stock under the constructive sale provisions of the Code;

- persons who hold or receive our common stock pursuant to the exercise of any employee stock option or otherwise as compensation; and

- tax-qualified retirement plans.

If a partnership (or other entity treated as a partnership for U.S. federal income tax purposes) holds our common stock, the tax treatment of a partner in the partnership will depend on the status of the partner, the activities of the partnership and certain determinations made at the partner level. Accordingly, partnerships holding our common stock and the partners in such partnerships should consult their tax advisors regarding the U.S. federal income tax consequences to them.

THIS DISCUSSION IS FOR INFORMATIONAL PURPOSES ONLY AND IS NOT TAX ADVICE. INVESTORS SHOULD CONSULT THEIR TAX ADVISORS WITH RESPECT TO THE APPLICATION OF THE U.S. FEDERAL INCOME TAX LAWS TO THEIR PARTICULAR SITUATIONS, AS WELL AS ANY TAX CONSEQUENCES OF THE PURCHASE, OWNERSHIP AND DISPOSITION OF OUR COMMON STOCK ARISING UNDER THE U.S. FEDERAL ESTATE OR GIFT TAX LAWS OR UNDER THE LAWS OF ANY STATE, LOCAL OR NON-U.S. TAXING JURISDICTION OR UNDER ANY APPLICABLE INCOME TAX TREATY.

Table of Contents

**Definition of a Non-U.S. Holder**

For purposes of this discussion, a non-U.S. holder is any beneficial owner of our common stock that is neither a U.S. person nor an entity treated as a partnership for United States federal income tax purposes. A U.S. person is any person that, for U.S. federal income tax purposes, is or is treated as any of the following:

- an individual who is a citizen or resident of the United States;
- a corporation (or other entity taxable as a corporation for U.S. federal income tax purposes) created or organized under the laws of the United States, any state thereof, or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income tax regardless of its source; or
- a trust that (1) is subject to the primary supervision of a U.S. court and the control of one or more United States persons (within the meaning of Section 7701(a)(30) of the Code), or (2) has made a valid election under applicable Treasury Regulations to continue to be treated as a United States person.

**Distributions**

As described in the section entitled Dividend Policy in this prospectus, we do not anticipate declaring or paying dividends to holders of our common stock in the foreseeable future. However, if we do make distributions of cash or property on our common stock, such distributions will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Amounts not treated as dividends for U.S. federal income tax purposes will constitute a return of capital and first be applied against and reduce a non-U.S. holder s tax basis in its common stock, but not below zero. Any excess will be treated as capital gain and will be treated as described below in the section relating to the sale or other taxable disposition of our common stock.

Subject to the discussion below on backup withholding and foreign accounts, dividends paid to a non-U.S. holder of our common stock that are not effectively connected with the non-U.S. holder s conduct of a trade or business within the United States will be subject to U.S. federal withholding tax at a rate of 30% of the gross amount of the dividends (or such lower rate specified by an applicable income tax treaty).

Non-U.S. holders will be entitled to a reduction in or an exemption from withholding on dividends as a result of either (a) an applicable income tax treaty or (b) the non-U.S. holder holding our common stock in connection with the conduct of a trade or business within the United States and dividends being paid in connection with that trade or business. To claim such a reduction in or exemption from withholding, the non-U.S. holder must provide the applicable withholding agent with a properly executed (a) IRS Form W-8BEN or W-8BEN-E claiming an exemption from or reduction of the withholding tax under the benefit of an income tax treaty between the United States and the country in which the non-U.S. holder resides or is established, or (b) IRS Form W-8ECI stating that the dividends are not subject to withholding tax because they are effectively connected with the conduct by the non-U.S. holder of a trade or business within the United States, as may be applicable. These certifications must be provided to the applicable withholding agent prior to the payment of dividends and must be updated periodically. Non-U.S. holders that do not timely provide the applicable withholding agent with the required certification, but that qualify for a

reduced rate under an applicable income tax treaty, may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS.

Subject to the discussion below on backup withholding and foreign accounts, if dividends paid to a non-U.S. holder are effectively connected with the non-U.S. holder s conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the non-U.S. holder maintains a permanent establishment in the United States to which such dividends are attributable), then, although exempt from U.S. federal withholding tax (provided the non-U.S. holder provides appropriate certification, as described above), the non-U.S. holder will be subject to U.S. federal income tax on such dividends on a net income basis at the regular graduated U.S. federal income tax rates. In addition, a non-U.S. holder that is a corporation may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on its effectively connected earnings and profits for the taxable year that are attributable to such dividends, as adjusted for certain items. Non-U.S. holders should consult their tax advisors regarding their entitlement to benefits under any applicable income tax treaty.

Table of Contents

**Sale or Other Taxable Disposition**

Subject to the discussions below on backup withholding and foreign accounts, a non-U.S. holder will not be subject to U.S. federal income tax on any gain realized upon the sale or other disposition of our common stock unless:

- the gain is effectively connected with the non-U.S. holder s conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the non-U.S. holder maintains a permanent establishment in the United States to which such gain is attributable);

- the non-U.S. holder is a nonresident alien individual present in the United States for 183 days or more during the taxable year of the disposition and certain other requirements are met; or

- our common stock constitutes a U.S. real property interest, or USRPI, by reason of our status as a U.S. real property holding corporation, or USRPHC, for U.S. federal income tax purposes.

Gain described in the first bullet point above will generally be subject to U.S. federal income tax on a net income basis at the regular graduated U.S. federal income tax rates. A non-U.S. holder that is a foreign corporation also may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) of a portion of its effectively connected earnings and profits for the taxable year, as adjusted for certain items.

A non-U.S. holder described in the second bullet point above will be subject to U.S. federal income tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on any gain derived from the disposition, which may be offset by certain U.S. source capital losses of the non-U.S. holder (even though the individual is not considered a resident of the United States) provided the non-U.S. holder has timely filed U.S. federal income tax returns with respect to such losses.

With respect to the third bullet point above, we believe we are not currently and do not anticipate becoming a USRPHC. Because the determination of whether we are a USRPHC depends on the fair market value of our USRPIs relative to the fair market value of our other business assets and our non-U.S. real property interests, however, there can be no assurance we are not a USRPHC or will not become one in the future. Even if we are or were to become a USRPHC, gain arising from the sale or other taxable disposition by a non-U.S. holder of our common stock will not be subject to U.S. federal income tax if such class of stock is regularly traded, as defined by applicable Treasury Regulations, on an established securities market, and such non-U.S. holder owned, actually or constructively, 5% or less of such class of our stock throughout the shorter of the five-year period ending on the date of the sale or other disposition or the non-U.S. holder s holding period for such stock.

Non-U.S. holders should consult their tax advisors regarding potentially applicable income tax treaties that may provide for different rules.

**Information Reporting and Backup Withholding**

A non-U.S. holder generally will not be subject to backup withholding with respect to payments of dividends on our common stock we make to the non-U.S. holder, provided the applicable withholding agent does not have actual knowledge or reason to know such holder is a U.S. person and the holder certifies its non-U.S. person status, such as by providing a valid IRS Form W-8BEN or W-8BEN-E or W-8ECI, or other applicable certification. However,

information returns will be filed with the IRS in connection with any dividends on our common stock paid to the non-U.S. holder, regardless of whether any tax was actually withheld. Copies of these information returns may also be made available under the provisions of a specific treaty or agreement to the tax authorities of the country in which the non-U.S. holder resides or is established.

Information reporting and backup withholding may apply to the proceeds of a sale of our common stock within the United States, and information reporting may (although backup withholding generally will not) apply to the proceeds of a sale of our common stock outside the United States conducted through certain U.S.-related financial intermediaries, in each case, unless the beneficial owner certifies under penalty of perjury that it is a non-U.S. holder on IRS Form W-8BEN or W-8BEN-E or other applicable form (and the payor does not have actual knowledge or reason to know that the beneficial owner is a U.S. person) or such owner otherwise establishes an exemption.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules may be allowed as a refund or a credit against a non-U.S. holder s U.S. federal income tax liability, provided the required information is timely furnished to the IRS.

Table of Contents

**Additional Withholding Tax on Payments Made to Foreign Accounts**

Withholding taxes may be imposed under Sections 1471 to 1474 of the Code (such Sections commonly referred to as the Foreign Account Tax Compliance Act, or FATCA) on certain types of payments made to non-U.S. financial institutions and certain other non-U.S. entities. Specifically, a 30% withholding tax may be imposed on dividends on, or gross proceeds from the sale or other disposition of, our common stock paid to a foreign financial institution or a non-financial foreign entity (each as defined in the Code), unless (1) the foreign financial institution undertakes certain diligence and reporting obligations, (2) the non-financial foreign entity either certifies it does not have any substantial United States owners (as defined in the Code) or furnishes identifying information regarding each substantial United States owner, or (3) the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from these rules. If the payee is a foreign financial institution and is subject to the diligence and reporting requirements in (1) above, it must enter into an agreement with the U.S. Department of the Treasury requiring, among other things, that it undertake to identify accounts held by certain specified United States persons or United States-owned foreign entities (each as defined in the Code), annually report certain information about such accounts, and withhold 30% on certain payments to non-compliant foreign financial institutions and certain other account holders. Foreign financial institutions located in jurisdictions that have an intergovernmental agreement with the United States governing FATCA may be subject to different rules.

The withholding provisions described above will generally apply to payments of dividends and will apply to payments of gross proceeds from a sale or other disposition of stock on or after January 1, 2017. Prospective investors should consult their tax advisors regarding the potential application of withholding under FATCA.

Table of Contents

## UNDERWRITING

Subject to the terms and conditions set forth in the underwriting agreement, dated July , 2015, between us and Jefferies LLC, as the representative of the underwriters named below and the sole book-running manager of this offering, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the respective number of shares of common stock shown opposite its name below:

| UNDERWRITER | NUMBER OF SHARES |
|---|---|
| Jefferies LLC | |
| Total | |

The underwriting agreement provides that the obligations of the several underwriters are subject to certain conditions precedent such as the receipt by the underwriters of officers certificates and legal opinions and approval of certain legal matters by their counsel. The underwriting agreement provides that the underwriters will purchase all of the shares of common stock if any of them are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the nondefaulting underwriters may be increased or the underwriting agreement may be terminated. We have agreed to indemnify the underwriters and certain of their controlling persons against certain liabilities, including liabilities under the Securities Act, and to contribute to payments that the underwriters may be required to make in respect of those liabilities.

The underwriters have advised us that, following the completion of this offering, they currently intend to make a market in the common stock as permitted by applicable laws and regulations. However, the underwriters are not obligated to do so, and the underwriters may discontinue any market-making activities at any time without notice in their sole discretion. Accordingly, no assurance can be given as to the liquidity of the trading market for the common stock, that you will be able to sell any of the common stock held by you at a particular time or that the prices that you receive when you sell will be favorable.

The underwriters are offering the shares of common stock subject to their acceptance of the shares of common stock from us and subject to prior sale. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

### Commission and Expenses

The underwriters have advised us that they propose to offer shares of common stock to the public at the initial public offering price set forth on the cover page of this prospectus and to certain dealers, which may include the underwriters, at that price less a concession not in excess of $ per share of common stock. The underwriters may

allow, and certain dealers may reallow, a discount from the concession not in excess of $ per share of common stock to certain brokers and dealers. After the offering, the initial public offering price, concession and reallowance to dealers may be reduced by the representative. No such reduction will change the amount of proceeds to be received by us as set forth on the cover page of this prospectus.

The following table shows the public offering price, the underwriting discounts and commissions that we are to pay the underwriters and the proceeds, before expenses, to us in connection with this offering. Such amounts are shown assuming both no exercise and full exercise of the underwriters option to purchase additional shares.

| | PER SHARE | | TOTAL | |
|---|---|---|---|---|
| | WITHOUT OPTION TO PURCHASE ADDITIONAL SHARES | WITH OPTION TO PURCHASE ADDITIONAL SHARES | WITHOUT OPTION TO PURCHASE ADDITIONAL SHARES | WITH OPTION TO PURCHASE ADDITIONAL SHARES |
| Public offering price | $ | $ | $ | $ |
| Underwriting discounts and commissions paid by us | $ | $ | $ | $ |
| Proceeds to us, before expenses | $ | $ | $ | $ |

Table of Contents

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately $ . We have also agreed to reimburse the underwriters up to an aggregate of $20,000 for certain expenses as set forth in the underwriting agreement.

**Listing**

Our common stock is listed on The NASDAQ Capital Market under the trading symbol CYTR.

**Stamp Taxes**

If you purchase shares of common stock offered in this prospectus supplement, you may be required to pay stamp taxes and other charges under the laws and practices of the country of purchase, in addition to the offering price listed on the cover page of this prospectus supplement.

**Option to Purchase Additional Shares**

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus supplement, to purchase, from time to time, in whole or in part, up to an aggregate of shares from us at the public offering price set forth on the cover page of this prospectus supplement, less underwriting discounts and commissions. If the underwriters exercise this option, each underwriter will be obligated, subject to specified conditions, to purchase a number of additional shares proportionate to that underwriter s initial purchase commitment as indicated in the table above.

**No Sales of Similar Securities**

We and each of our officers and directors have agreed, subject to specified exceptions, not to directly or indirectly:

- sell, offer, contract or grant any option to sell (including any short sale), pledge, transfer, establish an open put equivalent position within the meaning of Rule 16a-l(h) under the Securities Exchange Act of 1934, as amended, or

- otherwise dispose of any shares of common stock, options or warrants to acquire shares of common stock, or securities exchangeable or exercisable for or convertible into shares of common stock currently or hereafter owned either of record or beneficially, or

- publicly announce an intention to do any of the foregoing for a period of 90 days after the date of this prospectus supplement without the prior written consent of Jefferies LLC.

This restriction terminates after the close of trading of the common stock on and including the 90th day after the date of this prospectus supplement. However, subject to certain exceptions, in the event that either:

- during the last 17 days of the 90-day restricted period, we issue an earnings release or material news or a material event relating to us occurs, or

- prior to the expiration of the 90-day restricted period, we announce that we will release earnings results during the 16-day period beginning on the last day of the 90-day restricted period,

- prior to the expiration of the 90-day restricted period, we announce that we will release earnings results during the 16-day period beginning on the last day of the 90-day restricted period,

then in either case the expiration of the 90-day restricted period will be extended until the expiration of the 18-day period beginning on the date of the issuance of an earnings release or the occurrence of the material news or event, as applicable, unless Jefferies LLC waives, in writing, such an extension.

Jefferies LLC may, in its sole discretion and at any time or from time to time before the termination of the 90-day period release all or any portion of the securities subject to lock-up agreements.

Table of Contents

**Stabilization**

The underwriters have advised us that they, pursuant to Regulation M under the Securities Exchange Act of 1934, as amended, certain persons participating in the offering may engage in short sale transactions, stabilizing transactions, syndicate covering transactions or the imposition of penalty bids in connection with this offering. These activities may have the effect of stabilizing or maintaining the market price of the common stock at a level above that which might otherwise prevail in the open market. Establishing short sales positions may involve either covered short sales or naked short sales.

Covered short sales are sales made in an amount not greater than the underwriters option to purchase additional shares of our common stock in this offering. The underwriters may close out any covered short position by either exercising their option to purchase additional shares of our common stock or purchasing shares of our common stock in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option to purchase additional shares.

Naked short sales are sales in excess of the option to purchase additional shares of our common stock. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the shares of our common stock in the open market after pricing that could adversely affect investors who purchase in this offering.

A stabilizing bid is a bid for the purchase of shares of common stock on behalf of the underwriters for the purpose of fixing or maintaining the price of the common stock. A syndicate covering transaction is the bid for or the purchase of shares of common stock on behalf of the underwriters to reduce a short position incurred by the underwriters in connection with the offering. Similar to other purchase transactions, the underwriters purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. A penalty bid is an arrangement permitting the underwriters to reclaim the selling concession otherwise accruing to a syndicate member in connection with the offering if the common stock originally sold by such syndicate member are purchased in a syndicate covering transaction and therefore have not been effectively placed by such syndicate member.

Neither we, nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. The underwriters are not obligated to engage in these activities and, if commenced, any of the activities may be discontinued at any time.

The underwriters may also engage in passive market making transactions in our common stock on The NASDAQ Capital Market in accordance with Rule 103 of Regulation M during a period before the commencement of offers or sales of shares of our common stock in this offering and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker s bid, that bid must then be lowered when specified purchase limits are exceeded.

**Electronic Distribution**

A prospectus in electronic format may be made available by e-mail or on the web sites or through online services maintained by one or more of the underwriters or their affiliates. In those cases, prospective investors may view

offering terms online and may be allowed to place orders online. The underwriters may agree with us to allocate a specific number of shares of common stock for sale to online brokerage account holders. Any such allocation for online distributions will be made by the underwriters on the same basis as other allocations. Other than the prospectus supplement in electronic format, the information on the underwriters web sites and any information contained in any other web site maintained by any of the underwriters is not part of this prospectus supplement, has not been approved and/or endorsed by us or the underwriters and should not be relied upon by investors.

Table of Contents

**Other Activities and Relationships**

The underwriters and certain of their affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. The underwriters and certain of their affiliates have, from time to time, performed, and may in the future perform, various commercial and investment banking and financial advisory services for us and our affiliates, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and certain of their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers, and such investment and securities activities may involve securities and/or instruments issued by us and our affiliates. If the underwriters or their respective affiliates have a lending relationship with us, they routinely hedge their credit exposure to us consistent with their customary risk management policies. The underwriters and their respective affiliates may hedge such exposure by entering into transactions which consist of either the purchase of credit default swaps or the creation of short positions in our securities or the securities of our affiliates, including potentially the common stock offered hereby. Any such short positions could adversely affect future trading prices of the common stock offered hereby. The underwriters and certain of their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

**Disclaimers About Non-U.S. Jurisdictions**

***European Economic Area***

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State), each underwriter has represented and agreed that with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State (the Relevant Implementation Date) it has not made and will not make an offer of shares to the public in that Relevant Member State prior to the publication of a prospectus in relation to the shares which has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the competent authority in that Relevant Member State, all in accordance with the Prospectus Directive, except that it may, with effect from and including the Relevant Implementation Date, make an offer of shares to the public in that Relevant Member State at any time:

(a) to legal entities which are authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities;

(b) to any legal entity which has two or more of (1) an average of at least 250 employees during the last financial year; (2) a total balance sheet of more than 43,000,000 and (3) an annual net turnover of more than 50,000,000, as shown in its last annual or consolidated accounts;

(c) to fewer than 100 natural or legal persons (other than qualified investors as defined in the Prospectus Directive) subject to obtaining the prior consent of the representatives for any such offer; or

(d) in any other circumstances which do not require the publication by the Issuer of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an offer of shares to the public in relation to any shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the shares to be offered so as to enable an investor to decide to purchase or subscribe the shares, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State and the expression Prospectus Directive means Directive 2003/71/EC and includes any relevant implementing measure in each Relevant Member State.

Table of Contents

***United Kingdom***

This prospectus is only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive that are also (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended, referred to herein as the Order, and/or (ii) high net worth entities falling within Article 49(2)(a) to (d) of the Order and other persons to whom it may lawfully be communicated. Each such person is referred to herein as a Relevant Person.

This prospectus and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a Relevant Person should not act or rely on this document or any of its contents.

***Hong Kong***

The shares may not be offered or sold by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap.32, Laws of Hong Kong), or (ii) to professional investors within the meaning of the Securities and Futures Ordinance (Cap.571, Laws of Hong Kong) and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a prospectus within the meaning of the Companies Ordinance (Cap.32, Laws of Hong Kong), and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to professional investors within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder.

***Japan***

The securities have not been and will not be registered under the Financial Instruments and Exchange Law of Japan (the Financial Instruments and Exchange Law) and each underwriter has agreed that it will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and Exchange Law and any other applicable laws, regulations and ministerial guidelines of Japan.

***Singapore***

This prospectus supplement has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus supplement and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may they be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or the SFA, (ii) to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares are subscribed or purchased under Section 275 by a relevant person which is: (a) a corporation (which is not an accredited investor) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor, shares, debentures and units of shares and debentures of that corporation or the beneficiaries rights and interest in that trust shall not be transferable for 6 months after that corporation or that trust has acquired the shares under Section 275 except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA; (2) where no consideration is given for the transfer; or (3) by operation of law.

Table of Contents

***Switzerland***

The securities may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This prospectus has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art.1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this prospectus nor any other offering or marketing material relating to the securities or the offering may be publicly distributed or otherwise made publicly available in Switzerland. Neither this prospectus nor any other offering or marketing material relating to the offering, the Company or the securities have been or will be filed with or approved by any Swiss regulatory authority. In particular, this prospectus will not be filed with, and the offer of securities will not be supervised by, the Swiss Financial Market Supervisory Authority and the offer of securities has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of securities.

Table of Contents

## LEGAL MATTERS

The validity of the common stock offered hereby will be passed upon for us by TroyGould PC, Los Angeles, California. TroyGould PC owns 10,000 shares of our common stock as of the date of this prospectus supplement. Certain legal matters in connection with this offering will be passed upon for the underwriters by Latham & Watkins LLP, San Diego, California.

Table of Contents

## EXPERTS

Our consolidated financial statements and schedule as of December 31, 2014 and 2013 and for each of the three years in the period ended December 31, 2014 and management s assessment of the effectiveness of internal control over financial reporting as of December 31, 2014 incorporated by reference in this prospectus supplement have been so incorporated in reliance on the reports of BDO USA, LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

Table of Contents

## WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC s website at http://www.sec.gov. The SEC s website contains reports, proxy and information statements and other information regarding issuers, such as us, that file electronically with the SEC. You may also read and copy any document we file with the SEC at the SEC s Public Reference Room at 100 F Street, N.E., Room 1580, Washington, D.C., 20549. You may also obtain copies of these documents at prescribed rates by writing to the SEC. Please call the SEC at 1-800-SEC-0330 for further information on the operation of its Public Reference Room. Information on our website is not incorporated into this prospectus supplement and is not a part of this prospectus supplement.

Table of Contents

## INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

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

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

- our Annual Report on Form 10-K for the year ended December 31, 2014, filed with the SEC on March 10, 2015;
- our Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2015, filed with the SEC on May 1, 2015;
- our Current Reports on Form 8-K, filed with the SEC on January 6, 2015, March 11, 2015, May 1, 2015, June 24, 2015 and July 20, 2015;
- the description of our securities as described in our Registration Statement on Form 8-A filed under the Exchange Act on March 17, 1987 (File No. 0-15327), and any amendment or report filed for the purpose of updating any such description; and
- the description of our Series A Junior Participating Preferred Stock Purchase Rights as described in our Registration Statement on Form 8-A filed under the Exchange Act on April 17, 1997 (File No. 000-15327), and any amendment or report filed for the purpose of updating any such descriptions.

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

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

We will provide without charge upon written or oral request to each person, including any beneficial owner, to whom a prospectus supplement is delivered, a copy of any or all of the documents which are incorporated by reference into this prospectus supplement but not delivered with the prospectus (other than exhibits to those documents unless such exhibits are specifically incorporated by reference as an exhibit in this prospectus supplement). Requests should be directed to:

CytRx Corporation

11726 San Vicente Blvd.

Suite 650

Los Angeles, California 90049

Attention: Corporate Secretary

(310) 826-5648

Table of Contents

**PROSPECTUS**

**$100,000,000**

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

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

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

**An investment in our securities involves significant risks. Before purchasing any securities, you should consider carefully the risks referred to under Risk Factors on page B-8 in this prospectus and in the prospectus supplement.**

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

The date of this prospectus is December 23, 2013

Table of Contents

## TABLE OF CONTENTS

Table of Contents

## ABOUT THIS PROSPECTUS

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

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

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

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

Table of Contents

## NOTE ON FORWARD-LOOKING STATEMENTS

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

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

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

Table of Contents

## 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 B-6 of this prospectus. These and other factors could cause our future performance to differ materially from our assumptions and estimates.

Table of Contents

## ABOUT CYTRX

### 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 are conducting a global Phase 2b clinical trial with aldoxorubicin 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 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 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 aldoxorubicin as a therapy for patients with soft tissue sarcoma whose tumors have progressed following treatment with chemotherapy. We also are initiating Phase 2 clinical trials with aldoxorubicin in patients with late-stage glioblastoma (brain cancer) and 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:

| TECHNOLOGY | PRODUCT CANDIDATE | INDICATION(S) | STAGE OF DEVELOPMENT |
|---|---|---|---|
| Doxorubicin conjugate | Aldoxorubicin | Soft tissue sarcoma | Phase 3 1Q14 |
| | | | Phase 2b ongoing |
| | | Glioblastoma multiforme | Phase2 4Q13 |
| | | Kaposi s sarcoma | Phase2 4Q13 |
| | | In combination with doxorubicin in patients with advanced solid tumors | 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 cirulating abumin 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.

Table of Contents

*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.

Table of Contents

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.

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 plan to initiate in 2013 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.

Table of Contents

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 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, 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.

Table of Contents

## RISK FACTORS

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

### Risks Associated With Our Business

***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,

Table of Contents

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.

***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 a 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.

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 it 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

Table of Contents

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.

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.

Table of Contents

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

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

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

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

- we may become involved in time-consuming and expensive litigation, even if the claim is without merit;
- we may become liable for substantial damages for past infringement if a court decides that our technology infringes a competitor s patent;
- a court may prohibit us from selling or licensing our product without a license from the patent holder, which may not be available on commercially acceptable terms, if at all, or which may require us to pay substantial royalties or grant cross licenses to our patents; and
- we may have to redesign our product candidates or technology so that it does not infringe patent rights of others, which may not be possible or commercially feasible.

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

***Any 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.

Table of Contents

***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 Threshhold 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 Tracon 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.

As a result, these competitors may:

- succeed in developing competitive products sooner than us or our strategic partners or licensees;
- obtain FDA or foreign governmental approvals for their products before we can obtain approval of any of our products;
- 

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

- develop products that are safer or more effective than our products;
- devote greater resources than us to marketing or selling products;
- introduce or adapt more quickly than us to new technologies and other scientific advances;
- introduce products that render our products obsolete;
- withstand price competition more successfully than us or our strategic partners or licensees;
- negotiate third-party strategic alliances or licensing arrangements more effectively than us; and
- take better advantage than us of other opportunities.

Table of Contents

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

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

- commercially reasonable royalties based on a percentage of net sales (as defined in the agreement);
- a percentage of non-royalty sub-licensing income (as defined in the agreement); and
- milestones of $1,000,000 for each additional final marketing approval that we might obtain.

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

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

- commercially reasonable royalties based on a percentage of net sales (as defined in the agreement), dependent on reaching certain revenue thresholds;
- annual minimum payments if sales of bafetinib do not meet specified levels; and
- a percentage of non-royalty sub-licensing income (as defined in the agreement).

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

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

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

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

Table of Contents

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

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

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

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

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

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

- foreign regulatory requirements that could restrict or limit our ability to conduct our clinical trials;
- administrative burdens of conducting clinical trials under multiple foreign regulatory schema;
- foreign exchange fluctuations;
- diminished protection of intellectual property in some countries; and
- possible nationalization and expropriation.

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

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

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

**Risks Associated With Ownership of Our Common Stock**

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

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

Table of Contents

***We may experience volatility in our stock price, which may adversely affect the trading price of our common stock.***

The market price of our common stock has ranged from a low of $1.83 to a high of $3.65 per share from January 1, 2013 through November 26, 2013, and it may continue to experience significant volatility from time to time. Factors that may affect the market price of our common stock include the following:

- announcements of regulatory developments or technological innovations by us or our competitors;
- changes in our relationship with our licensors and other strategic partners;
- our quarterly operating results;
- litigation involving or affecting us;
- shortfalls in our actual financial results compared to our guidance or the forecasts of stock market analysts;
- developments in patent or other technology ownership rights;
- acquisitions or strategic alliances by us or our competitors;
- public concern regarding the safety of our products; and
- government regulation of drug pricing.

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

As of September 30, 2013, there were outstanding stock options to purchase approximately 3.4 million shares of our common stock at a weighted-average exercise price of $4.15 per share and outstanding warrants to purchase approximately 1.6 million shares of common stock at a weighted-average exercise price of $6.58 per share. Our outstanding options and warrants could adversely affect our ability to obtain future financing or engage in certain mergers or other transactions, since the holders of options and warrants can be expected to exercise them at a time when we may be able to obtain additional capital through a new offering of securities on terms more favorable to us than the terms of outstanding options and warrants. For the life of the options and warrants, the holders have the opportunity to profit from a rise in the market price of our common stock without assuming the risk of ownership. The issuance of shares upon the exercise of outstanding options and warrants will also dilute the ownership interests of our existing stockholders.

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

***Our anti-takeover measures may make it more difficult to change our management, or may discourage others from acquiring us, and thereby adversely affect stockholder value.***

We have a stockholder rights plan and provisions in our bylaws that are intended to protect our stockholders interests by encouraging anyone seeking control of our company to negotiate with our board of directors. These provisions may discourage or prevent a person or group from acquiring us without the approval of our board of directors, even if the acquisition would be beneficial to our stockholders.

We have a classified board of directors, which means that at least two stockholder meetings, instead of one, will be required to effect a change in the majority control of our board of directors. This applies to every election of directors, not just an election occurring after a change in control. The classification of our board increases the amount of time it takes to change majority control of our board of directors and may cause potential acquirers to lose interest in a potential purchase of us, regardless of whether our purchase would be beneficial to us or our stockholders. The additional time and cost to change a majority of the members of our board of directors makes it more difficult and may discourage our existing stockholders from seeking to change our existing management in order to change the strategic direction or operational performance of our company.

Our bylaws provide that directors may only be removed for cause by the affirmative vote of the holders of at least a majority of the outstanding shares of our capital stock then entitled to vote at an election of directors. This provision prevents stockholders from removing any incumbent director without cause. Our bylaws also provide that a stockholder must give us at least 120 days notice of a proposal or director nomination that such stockholder desires to present at any annual meeting or special meeting of stockholders. Such provision prevents a stockholder from making a proposal or director nomination at a stockholder meeting without us having advance notice of that proposal

Table of Contents

or director nomination. This could make a change in control more difficult by providing our directors with more time to prepare an opposition to a proposed change in control. By making it more difficult to remove or install new directors, these bylaw provisions may also make our existing management less responsive to the views of our stockholders with respect to our operations and other issues such as management selection and management compensation.

We are subject to the anti-takeover provisions of Section 203 of the Delaware General Corporation Law, which may also prevent or delay a takeover of us that may be beneficial to our stockholders.

***Our amended and restated by-laws designate the Court of Chancery of the State of Delaware as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders ability to obtain a favorable judicial forum for disputes with us or our directors, officers or other employees.***

Our amended and restated by-laws provide that, unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any director, officer or other employee to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, or (iv) any action asserting a claim that is governed by the internal affairs doctrine. Any person purchasing or otherwise acquiring any interest in any shares of our capital stock shall be deemed to have notice of and to have consented to this provision of our amended and restated by-laws. This choice-of-forum provision may limit our stockholders ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits. Alternatively, if a court were to find this provision of our amended and restated by-laws inapplicable or unenforceable with respect to one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could adversely affect our business and financial condition.

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

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

***We do not expect to pay any cash dividends on our common stock.***

We have not declared or paid any cash dividends on our common stock or other securities, and we currently do not anticipate paying any cash dividends in the foreseeable future. Because we do not anticipate paying cash dividends for the foreseeable future, our stockholders will not realize a return on their investment in our common stock except to the extent of any appreciation in the value of our common stock. Our common stock may not appreciate in value, or may decline in value.

Table of Contents

## USE OF PROCEEDS

Unless we state otherwise in the accompanying prospectus supplement, we intend to use the net proceeds from the sale of securities offered by this prospectus for working capital and general corporate purposes, including the clinical trials of our product candidates. General corporate purposes also may include repayment of our existing indebtedness, financing of capital expenditures and future acquisitions and strategic investments.

We have not determined the amounts we plan to spend on any of the areas listed above or the timing of these expenditures. As a result, our management will have broad discretion to allocate the net proceeds from this offering. Pending application of the net proceeds as described above, we expect to invest the net proceeds in short-term, interest-bearing, investment-grade securities pursuant to our investment policy.

Table of Contents

## FINANCIAL RATIOS

The following table sets forth our ratio of earnings, if any, to fixed charges for each of the periods presented:

| | YEAR ENDED DECEMBER 31 | | | | | |
|---|---|---|---|---|---|---|
| | 2008 | 2009 | 2010 | 2011 | 2012 | THREE MONTHS ENDED SEPTEMBER 30, 2013 |
| Ratio of earnings to fixed charges [1][2] | | | | | | |
| Deficiency of earnings available to cover fixed charges | | | | | | |

(1) *Fixed charges*. The term fixed charges means the sum of the following, if any: (a) interest expensed and capitalized, (b) amortized premiums, discounts and capitalized expenses related to indebtedness, (c) an estimate of the interest within rental expense, and (d) preference security dividend requirements of consolidated subsidiaries. *Earnings*. The term earnings is the amount resulting from adding and subtracting the following items, if any: Add the following: (a) pre-tax income from continuing operations before adjustment for income or loss from equity investees; (b) fixed charges; (c) amortization of capitalized interest; (d) distributed income of equity investees; and (e) our share of pre-tax losses of equity investees for which charges arising from guarantees are included in fixed charges. From the total of the added items, subtract the following: (a) interest capitalized; (b) preference security dividend requirements of consolidated subsidiaries; and (c) the noncontrolling interest in pre-tax income of subsidiaries that have not incurred fixed charges. Equity investees are investments that we account for using the equity method of accounting. The ratio of earnings to fixed charges is computed by dividing earnings by fixed charges as defined below, respectively.

(2) Our net losses were insufficient to cover fixed charges in the periods indicated. For this reason, the ratio information is not applicable.

Table of Contents

## DIVIDEND POLICY

Our board of directors sets our dividend policy. We have never paid any cash dividends on our common stock and do not intend to declare cash dividends on our common stock in the foreseeable future. We currently intend to retain all available funds and any future earnings for use in the operation and expansion of our business, but we may determine in the future to declare or pay cash dividends on our common stock. Any future determination as to the declaration and payment of dividends will be at the discretion of our board of directors and will be dependent upon our results of operations and cash flows, our financial position and capital requirements, general business conditions, legal, tax, regulatory and any contractual restrictions on the payment of dividends, and any other factors our board of directors deems relevant.

Table of Contents

## THE SECURITIES THAT WE MAY OFFER

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

- shares of our common stock, par value $.001 per share;
- shares of our preferred stock, par value $.01 per share;
- warrants to purchase our common stock or preferred stock; and
- any combination of the securities listed above, separately or as units, each on terms to be determined at the time of sale.

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

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

Table of Contents

## DESCRIPTION OF CAPITAL STOCK

As of November 26, 2013, our authorized capital stock consisted of 250,000,000 shares of common stock, $.001 par value per share, of which 41,975,412 shares were outstanding (exclusive of treasury shares), and 5,000,000 shares of preferred stock, $.01 par value per share, none of which was outstanding.

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

### Common Stock

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

### Preferred Stock

We are currently authorized to issue 5,000,000 shares of preferred stock, of which 25,000 shares have been designated as Series A Junior Participating Preferred Stock. We have reserved all of the shares of our Series A Junior Participating Preferred Stock for issuance upon the exercise of the rights under our Shareholder Protection Rights Agreement described below.

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

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

- the title and stated value;
- the number of shares we are offering;

- the liquidation preference per share;
- the purchase price per share;
- the dividend rate per share, dividend period, payment date or dates and method of calculation of dividends;
- whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- our right, if any, to defer payment of dividends and the maximum length of any such deferral period;
- the procedures for any auction and remarketing, if any;
- the provisions for a sinking fund, if any;
- the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;
- any listing of the preferred stock on any securities exchange or market;

Table of Contents

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

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

- voting rights, if any;

- preemptive rights, if any;

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

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

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

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

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

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

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

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

**Anti-Takeover Measures**

***Delaware Law***

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

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

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

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

Except as specified in Section 203, an interested stockholder is generally defined to include any person who, together with any affiliates or associates of that person, beneficially owns, directly or indirectly, 15% or more of the outstanding voting stock of the corporation, or is an affiliate or associate of the corporation and was the owner of 15% or more of the outstanding voting stock of the corporation, any time within three years immediately prior to the relevant date. Under certain circumstances, Section 203 makes it more difficult for an interested stockholder to effect various business combinations with a corporation for a three-year period, although the stockholders may elect

Table of Contents

not to be governed by this section, by adopting an amendment to the certificate of incorporation or by-laws, effective 12 months after adoption. Our amended and restated certificate of incorporation and by-laws do not opt out from the restrictions imposed under Section 203. We anticipate that the provisions of Section 203 may encourage companies interested in acquiring us to negotiate in advance with the board because the stockholder approval requirement would be avoided if a majority of the directors then in office excluding an interested stockholder approve either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder. These provisions may have the effect of deterring hostile takeovers or delaying changes in control, which could depress the market price of our common stock and deprive stockholders of opportunities to realize a premium on shares of common stock held by them.

***Charter and By-Law Provisions***

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

- our restated by-laws classify the board of directors into three classes with staggered three-year terms;
- under our restated by-laws, our board of directors may enlarge the size of the board and fill the vacancies;
- our restated by-laws provide that a stockholder may not nominate candidates for the board of directors at any annual or special meeting unless that stockholder notifies us of its intention a specified period in advance and provides us with certain required information;
- stockholders who wish to bring business before the stockholders at our annual meeting must provide advance notice; and
- our restated by-laws provide that special meetings of stockholders may only be called by our board of directors or by an officer so instructed by our board.

Our restated by-laws also provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for:

- any derivative action or proceeding brought on our behalf;
- any action asserting a claim of breach of a fiduciary duty owed by any director, officer or other employee of the company to us or our stockholders;
- any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law; or

- any action asserting a claim governed by the internal affairs doctrine.

Our restated by-laws further provide that any person or entity purchasing or otherwise acquiring any interest in shares of capital stock of the company is deemed to have notice of and consented to the foregoing provision.

***Shareholder Protection Rights Agreement***

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

**Transfer Agent**

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

Table of Contents

## DESCRIPTION OF WARRANTS

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

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

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

- the title of the warrants;
- the common stock or preferred stock for which the warrants are exercisable;
- the price at which the warrants will be issued and the exercise price of the warrants;
- the aggregate number of warrants offered;
- the number of shares of common stock or preferred stock that may be purchased upon the exercise of each warrant;
- whether the warrants are being offered separately or as a part of units consisting of shares of our common stock or preferred stock and warrants to purchase additional shares of our common stock or preferred stock;
- the terms of any right by us to redeem the warrants;
- the date on which the right to exercise the warrants will commence and the date on which this right will expire;
- the procedures for exercising the warrants;

- the terms on which the warrants may be amended;

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

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

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

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

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

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

Table of Contents

## DESCRIPTION OF UNITS

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

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

- the price of each unit;
- the securities comprising each unit;
- the exercise price of the warrants comprising part of the units;
- the aggregate number of units offered;
- the number of shares of common stock or preferred stock that may be purchased upon the exercise of each warrant comprising part of a unit;
- the terms of any right by us to redeem any of the securities comprising the units;
- the date on which the right to exercise the warrants forming part of the units will commence and the date on which this right will expire;
- any transfer restrictions on the units, including whether the securities comprising the units may be transferred separately;
- the terms on which the units or warrants forming part of the units may be amended;
- with respect to preferred stock forming part of the units, the other matters listed above under Description of Capital Stock Preferred Stock ;

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

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

Table of Contents

## PLAN OF DISTRIBUTION

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

- through agents to the public or to investors;
- to one or more underwriters for resale to the public or to investors;
- in at the market offerings, within the meaning of Rule 415(a)(4) of the Securities Act of 1933, as amended, or the Securities Act, to or through a market maker or into an existing trading market, on an exchange or otherwise;
- directly to investors; or
- through a combination of these methods of sale.

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

- the name or names of any agents or underwriters;
- the purchase price of the securities being offered and the proceeds we will receive from the sale;
- any over-allotment options under which underwriters may purchase additional securities from us;
- any agency fees or underwriting discounts and other items constituting agents or underwriters compensation;
- the public offering price; and
- any discounts or concessions allowed or reallowed or paid to dealers.

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

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

- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

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

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

To facilitate the offering of securities, certain persons participating in the offering may engage in transactions that stabilize, maintain, or otherwise affect the price of the securities. This may include over-allotments or short sales of the securities, which involve the sale by persons participating in the offering of more securities than we sold to them. In these circumstances, these persons would cover such over-allotments or short positions by making purchases in the open market or by exercising their over-allotment option, if any. In addition, these persons may stabilize or maintain the price of the securities by bidding for or purchasing securities in the open market or by imposing penalty

bids, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if securities sold by them is repurchased in connection with stabilization transactions. The effect of these transactions may be to stabilize or maintain the market price of the securities at a level above that which might otherwise prevail in the open market. These transactions may be discontinued at any time.

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

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

Table of Contents

## WHERE YOU CAN FIND MORE INFORMATION

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

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

Table of Contents

## INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

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

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

- our Annual Report on Form 10-K for the year ended December 31, 2012;
- our Quarterly Reports on Form 10-Q for the quarterly periods ended March 31, 2013, June 30, 2013 and September 30, 2013, respectively;
- our Current Reports on Form 8-K filed with the SEC on January 3, 2013, March 11, 2013, May 9, 2013, July 16, 2013, August 6, 2013, October 9, 2013 and October 29, 2013, respectively;
- the description of our securities as described in our Registration Statement on Form 8-A filed under the Exchange Act on March 17, 1987 (File No. 0 15327), and any amendment or report filed for the purpose of updating any such description; and
- the description of our Series A Junior Participating Preferred Stock Purchase Rights as described in our Registration Statement on Form 8-A filed under the Exchange Act on April 17, 1997 (File No. 000 15327), and any amendment or report filed for the purpose of updating any such descriptions.

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

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

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

B-30

Table of Contents

## LEGAL MATTERS

The validity of the securities being offered hereby has been passed upon for us by TroyGould PC, Los Angeles, California.

Table of Contents

## EXPERTS

The consolidated financial statements and schedules as of December 31, 2012 and 2011 and for each of the three years in the period ended December 31, 2012 and management s assessment of the effectiveness of internal control over financial reporting as of December 31, 2012 incorporated by reference in this prospectus have been so incorporated in reliance on the reports of BDO USA, LLP, an independent registered public accounting firm, incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

Table of Contents

**Shares**

Common Stock

**PROSPECTUS SUPPLEMENT**

*Sole Book-Running Manager*

**Jefferies**

July , 2015