

CYTRX CORP
Form 424B2
July 15, 2016
Table of Contents

Filed Pursuant to Rule 424(b)(2)
Registration No. 333-208803

THE INFORMATION IN THIS PRELIMINARY PROSPECTUS SUPPLEMENT AND THE ACCOMPANYING PROSPECTUS IS NOT COMPLETE AND MAY BE CHANGED. THIS PRELIMINARY PROSPECTUS 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 14, 2016

PRELIMINARY PROSPECTUS SUPPLEMENT

(To Prospectus dated June 17, 2016)

Shares of Common Stock

Warrants to Purchase

Shares of Common Stock

We are offering _____ shares of our common stock and warrants to purchase up to _____ shares of our common stock at an exercise price of \$ _____ per whole share of common stock. The shares of common stock and warrants will be sold in units, with each unit consisting of one share of common stock and a warrant to purchase _____ of a share of common stock. Each unit will be sold at a price of \$ _____ per unit. The shares of common stock and warrants will be mandatorily separable immediately upon issuance.

Our common stock is listed on The NASDAQ Capital Market under the symbol CYTR. On July 13, 2016 the last reported sale price of our common stock on The NASDAQ Capital Market was \$0.899 per share.

The warrants are not and will not be listed for trading on The NASDAQ Capital Market, or any other securities exchange or nationally recognized trading system. There is no market through which the warrants may be sold, and purchasers may not be able to resell the warrants purchased under this prospectus supplement. This may affect the pricing of the warrants in the secondary market, the transparency and availability of trading prices, and the liquidity of the warrants.

Investing in our securities involves a high degree of risk. Please read Risk Factors beginning on page S-9 of this prospectus supplement 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 UNIT	TOTAL
Public offering price	\$	\$
Placement agent fees ⁽¹⁾	\$	\$
Proceeds to CytRx Corporation before expenses	\$	\$

(1) In addition, we have agreed to pay the placement agent a management fee equal to 1% of the gross proceeds of this offering and to reimburse the placement agent for offering expenses in the non-accountable sum of \$25,000 and for legal fees and expenses in the non-accountable sum of \$100,000. See the Plan of Distribution section of this prospectus for more information on the placement agent arrangements.

We have engaged H.C. Wainwright & Co., LLC (Wainwright or the Placement Agent) to act as our exclusive placement agent in connection with this offering. Wainwright is not purchasing or selling the securities offered by us, and is not required to sell any specific number or dollar amount of securities, but will use its reasonable best efforts to arrange for the sale of the securities offered. We have agreed to pay Wainwright a placement fee equal to 6% of the aggregate gross proceeds to us from the sale of the securities in the offering. Wainwright may engage one or more sub-agents or selected dealers in connection with this offering. We estimate total expenses of this offering, excluding the placement agent fees, will be approximately \$. Because there is no minimum offering amount required as a condition to closing in this offering, the actual public offering amount, placement agent fees, and proceeds to us, if any, are not presently determinable and may be substantially less than the total maximum offering amounts set forth above. This offering will terminate on July , 2016, unless the offering is fully subscribed before that date or we decide to terminate the offering prior to that date. In either event, the offering may be closed without further notice to you. We have not arranged to place the funds from investors in an escrow, trust or similar account.

Rodman & Renshaw
a unit of H.C. Wainwright & Co.
Prospectus Supplement dated July , 2016

Table of Contents

TABLE OF CONTENTS
PROSPECTUS SUPPLEMENT

	PAGE
<u>ABOUT THIS PROSPECTUS SUPPLEMENT</u>	S-1
<u>NOTE ON FORWARD-LOOKING STATEMENTS</u>	S-1
<u>INDUSTRY DATA</u>	S-2
<u>TRADEMARKS</u>	S-2
<u>SUMMARY OF PROSPECTUS SUPPLEMENT</u>	S-3
<u>RISK FACTORS</u>	S-9
<u>USE OF PROCEEDS</u>	S-26
<u>DIVIDEND POLICY</u>	S-26
<u>CAPITALIZATION</u>	S-26
<u>DILUTION</u>	S-27
<u>DESCRIPTION OF OUR SECURITIES</u>	S-28
<u>PLAN OF DISTRIBUTION</u>	S-31
<u>LEGAL MATTERS</u>	S-33
<u>EXPERTS</u>	S-33
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	S-33
<u>INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE</u>	S-33

PROSPECTUS

	PAGE
<u>ABOUT THIS PROSPECTUS</u>	2
<u>NOTE ON FORWARD-LOOKING STATEMENTS</u>	2
<u>INDUSTRY DATA</u>	2
<u>TRADEMARKS</u>	3
<u>ABOUT CYTRX</u>	3
<u>RISK FACTORS</u>	12
<u>USE OF PROCEEDS</u>	12
<u>FINANCIAL RATIOS</u>	12
<u>DIVIDEND POLICY</u>	13
<u>THE SECURITIES THAT WE MAY OFFER</u>	13
<u>DESCRIPTION OF CAPITAL STOCK</u>	13
<u>DESCRIPTION OF WARRANTS</u>	16
<u>DESCRIPTION OF UNITS</u>	17
<u>PLAN OF DISTRIBUTION</u>	18
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	19
<u>INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE</u>	19
<u>LEGAL MATTERS</u>	20
<u>EXPERTS</u>	20

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.

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 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, 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 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 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 of our securities, you should consider carefully all of the factors set forth or referred to in this prospectus supplement that could cause actual results to differ.

S-1

Table of Contents

INDUSTRY DATA

Unless otherwise indicated, information contained or incorporated by reference in this prospectus supplement 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 referred to under "Risk Factors" on page S-12 of this prospectus supplement. These and other factors could cause our future performance to differ materially from our assumptions and estimates.

TRADEMARKS

CytRx is one of our trademarks used in this prospectus supplement. This prospectus supplement also includes trademarks, trade names and service marks that are the property of other organizations. Solely for convenience, trademarks and trade names referred to in this prospectus supplement 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 OF PROSPECTUS SUPPLEMENT

Company Overview

CytRx Corporation (we, us, our or the company) is a biopharmaceutical research and development company specializing in oncology. We currently are focused on the clinical development of aldoxorubicin (formerly known as INNO-206), our modified version of the widely-used chemotherapeutic agent, doxorubicin. We recently announced an analysis from our on-going global, randomized Phase 3 clinical trial of aldoxorubicin as a treatment for patients with relapsed or refractory soft tissue sarcomas, or STS. The trial enrolled 433 patients at 79 sites in 15 countries including the U.S. and Canada.

The current evaluation did not show a statistically significant difference between aldoxorubicin and investigator's choice therapy for the primary endpoint of progression-free survival, or PFS, with a median of 4.17 months and 4.04 months, respectively (hazard ratio: 0.91). The objective response rate (ORR), which measures tumor shrinkage, and disease control rate (ORR + stable disease ³ 4 months), showed a near doubling in the aldoxorubicin arm compared to investigator's choice, including in patients who previously received treatment with doxorubicin. Disease control rate for aldoxorubicin was significantly greater than investigator's choice therapy in the intent-to-treat population (p=0.048) as well as in patients who received prior doxorubicin (p=0.0415). Patients continue to be followed for overall survival (OS), a secondary endpoint of the trial.

We have previously reported positive top-line efficacy results (median progression-free survival, progression-free survival 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 STS. Hazard ratios – the likelihood that the study endpoint (in this case tumor progression) will be reached during a given period – are an important measure of the reliability and uniformity of the absolute data for progression-free survival, or PFS. The trial investigated the efficacy and safety of aldoxorubicin compared with doxorubicin in subjects with first-line metastatic, locally advanced or unresectable STS. Aldoxorubicin combines the chemotherapeutic agent doxorubicin with a novel linker-molecule that binds specifically to albumin in the blood to allow for delivery of higher amounts of doxorubicin (3 ½ to 4 times) without the major dose-limiting toxicities seen with administration of doxorubicin alone.

We are currently evaluating aldoxorubicin in a global Phase 2b clinical trial in second-line small cell lung cancer, a Phase 2 clinical trial in patients with late-stage glioblastoma (brain cancer), a Phase 1b trial in combination with ifosfamide in patients with soft tissue sarcoma, and a Phase 1b trial in combination with gemcitabine in subjects with metastatic solid tumors. We have completed a global Phase 2b clinical trial with aldoxorubicin as a first-line therapy for STS, a Phase 1b/2 clinical trial primarily in the same indication, a Phase 2 clinical trial in HIV-related Kaposi's Sarcoma, 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.

In addition to aldoxorubicin, we are currently completing pre-clinical development for DK049, a novel anti-cancer drug conjugate that utilizes our Linker Activated Drug Release (LADR) technology. DK049 was created at our laboratory facility in Freiburg, Germany, and employs a proprietary linker that is both pH sensitive and requires a specific enzyme for the release of the cytotoxic payload. DK049 has demonstrated significant anti-tumor activity in multiple animal models implanted with human tumors, including non-small cell lung, ovarian and pancreatic cancers. We anticipate filing an Investigational New Drug Application (IND) in 2017.

We plan to expand our pipeline of oncology candidates utilizing our LADR technology by creating both albumin-binding drug conjugates and antibody-drug conjugates. This technology allows for targeting to the tumor either by albumin or antibodies and can deliver anti-cancer agents that are 10-1000 times more potent than traditional

chemotherapies.

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.

Technology	Product candidate	Indication(s)	Stage of Development
Doxorubicin conjugate	Aldoxorubicin	Soft Tissue Sarcoma Small-Cell Lung Cancer	Pivotal Global Phase 3 Global Phase 2b

S-3

Table of Contents

Technology	Product candidate	Indication(s)	Stage of Development
		Glioblastoma Multiforme	Phase 2
		Kaposi's Sarcoma	Phase 2
		Combination with ifosfamide	Phase 1b
		Combination with gemcitabine	Phase 1b
LADR™	DK049	To be announced	Pre-clinical
LADR™ for albumin-binding drug conjugates	To be announced	To be announced	Pre-clinical
LADR™ for antibody-drug conjugates	To be announced	To be announced	Pre-clinical

Our Clinical Development Programs

Our current clinical development programs are discussed below.

Aldoxorubicin

Aldoxorubicin is a conjugate of the commonly prescribed chemotherapeutic agent doxorubicin that binds to circulating albumin in the bloodstream and is believed to concentrate the drug 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, we initiated under an SPA granted by the FDA 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 certain 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

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, 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.

S-4

Table of Contents

We have also 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, 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 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 I 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 *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 ten of 13 (76.9%) evaluable patients with relapsed or refractory STS. The median number of cycles of aldoxorubicin administered at the maximum tolerable dose was eight. The results of this clinical trial were published in February 2015 in the peer-reviewed journal *Cancer* (*Cancer*, 2015 Feb 15; 121(4); 570-9).

In addition, best responses for the 13 evaluable STS trial subjects included the following: five (38.5%) achieved partial response, as defined as shrinkage of target tumors of more than 30%; six (46%) 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. Final observed median PFS for advanced STS patients in the trial was 11.25 months, and median overall survival was 21.71 months (Publication in *Cancer*, 2015 Feb 15). In addition, following 8 cycles of aldoxorubicin, two patients experienced no progression of disease for 23 and 15 months, respectively, despite no further treatment.

In connection with our Phase 1b pharmacokinetics clinical trial evaluating the pharmacokinetics and safety of aldoxorubicin in patients with metastatic solid tumors who have either relapsed or not responded to treatment with standard therapies, we announced data demonstrating that aldoxorubicin has a distribution half-life of approximately 20 to 24 hours, with a narrow volume of distribution to healthy tissue and slow clearance from the circulation. These characteristics distinguish aldoxorubicin from doxorubicin, which has a distribution half-life of about five minutes according to its package insert. Complete details from this Phase 1b trial were published online in the journal *Investigational New Drugs* in November 2014 (Publication in *Invest New Drugs*, 2015 Apr 15; (33(2):341-8).

We completed our global Phase 2b clinical trial to evaluate the preliminary efficacy and safety of aldoxorubicin as a first-line therapy in patients with advanced STS who are ineligible for surgery, 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 first-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 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 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

S-5

Table of Contents

CT scans to monitor tumor size. The primary endpoint was PFS as determined by a blinded radiology review performed at an independent central radiology laboratory. Secondary endpoints included overall response rates (complete and partial) and PFS at six months for each group, and overall survival. The results from this trial were published in the Journal of the American Medical Association (JAMA) Oncology in September 2015 (JAMA Oncol. 2015 Sep 17:1-9.).

The central radiology review, as well as the investigators' own assessments, showed an 80% to 100% improvement in PFS among patients treated with aldorubicin. In an intent-to-treat analysis, the investigator-assessed median PFS was 8.3 months for aldorubicin patients versus 4.6 months for doxorubicin patients ($p=0.0006$), while the blinded central radiology review indicated that median PFS for aldorubicin patients was 5.6 months versus 2.7 months for doxorubicin patients ($p=0.0228$). Per investigators, 68.1% of aldorubicin patients had not progressed at six months, compared with 33.0% of doxorubicin-treated patients ($p=0.008$). By blinded central radiology review, 45.7% of aldorubicin patients had not progressed at six months, compared with 22.9% of doxorubicin patients ($p=0.02$).

The overall response rate as determined by the investigators was 22.9% for aldorubicin subjects (2.0% complete response and 21.3% 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 aldorubicin subjects had a partial response while none of the doxorubicin subjects exhibited any objective response.

Additional analysis determined hazard ratios for the primary endpoint of PFS by both investigators at study sites and by the blinded radiology review. The hazard ratio for investigator-read scans is 0.37 (95% confidence interval, range of 0.212 to 0.643) ($p=0.0004$), reflecting a 63% reduction in the risk of disease progression for patients treated with aldorubicin; and the hazard ratio for central lab scans is 0.586 (95% confidence interval, range of 0.358 to 0.960) ($p=0.034$), reflecting a 41% reduction in the risk of disease progression for the aldorubicin-treated patients. Hazard ratios are an important measure of the reliability and uniformity of the data for PFS, and where the upper limit is less than one 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 analysis describes the time it takes for tumors to progress in individual patients, showed significant improvement in subjects treated with aldorubicin versus subjects treated with doxorubicin.

The overall survival results from the clinical trial demonstrated a 27 percent reduction in the risk of death compared to patients treated with doxorubicin (HR 0.73: 95% confidence interval 0.44-1.20), the current standard-of-care in this indication. In addition, aldorubicin-treated patients demonstrated a 41% likelihood of surviving more than 2 years, a 2-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 aldorubicin-treated patients versus 14.3 months (95% confidence interval 8.6-20.6) for doxorubicin treated patients ($p=0.21$). For treatment-naïve patients, representing 90% of the patients in the clinical trial, median overall survival was 15.8 months (95% confidence interval 13.0-not reached) for aldorubicin-treated patients versus 13.8 months (95% confidence interval 8.6-19.8) for doxorubicin treated patients ($p=0.14$).

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

In the first quarter of 2014, we initiated a pivotal global Phase 3 clinical trial to evaluate the efficacy and safety of aldoxorubicin as a second-line treatment for patients with STS under a Special Protocol Assessment with the FDA. This multicenter, randomized, open-label Phase 3 clinical trial is designed to enroll approximately 400 patients with metastatic, locally advanced or unresectable soft tissue sarcomas 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 progression-free survival (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 (defined as an increase in the size of measurable tumors by 20% or the development of a new tumor lesion), which creates the potential for substantially improved Phase 3 efficacy results.

Table of Contents

The clinical trial enrolled 433 patients at 79 clinical sites in the 15 countries including the U.S. and Canada. We recently announced an analysis from our on-going global, randomized Phase 3 clinical trial. The current evaluation did not show a statistically significant difference between aldoxorubicin and investigator's choice therapy for the primary endpoint of progression-free survival, or PFS, with a median of 4.17 months and 4.04 months, respectively (hazard ratio: 0.91). A high degree of patient censoring, nearly 50%, may have impacted this analysis. CytRx plans to conduct a future analysis to allow for a longer duration of follow up for patients enrolled in the trial. Although the PFS endpoint was not achieved, objective response rate (ORR), which measures tumor shrinkage, and disease control rate (ORR + stable disease ³ 4 months), showed a near doubling in the aldoxorubicin arm compared to investigator's choice, including in patients who previously received treatment with doxorubicin. Disease control rate for aldoxorubicin was significantly greater than investigator's choice therapy in the intent-to-treat population (p=0.048) as well as in patients who received prior doxorubicin (p=0.0415). Patients continue to be followed for overall survival (OS), a secondary endpoint of the trial. Following the future analysis of the Phase 3 trial capturing a longer duration of patient follow-up, CytRx intends to meet with the FDA to discuss the data and a possible regulatory path forward for aldoxorubicin as a treatment for patients with one or more subtypes of advanced STS.

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 (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) in the U.S., Spain and Hungary. The primary endpoint is PFS and the secondary endpoints are OS, overall response rates (partial and complete) and the safety of aldoxorubicin compared to topotecan in this population.

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 has enrolled its target of 28 patients at sites including the John Wayne Cancer Center in Santa Monica, California, City of Hope in Duarte, California, and the LSU Medical Center in New Orleans, Louisiana.

We have completed 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 U.S. 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 a Phase 1b trial in combination with ifosfamide in patients with STS, and a Phase 1b trial in combination with gemcitabine in subjects with metastatic solid tumors. Since most 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

Our laboratory, located in Freiburg, Germany, is conducting discovery and translational research to create drug candidates that utilize our LADR technologies to couple cytotoxic agents and proteins either inside the body or externally, and then concentrate 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 and using LADR linkers to create unique antibody-drug conjugates. We recently announced the development of DK049, a novel anti-cancer drug conjugate that

utilizes our LADR technology, and anticipate filing an IND for DK049 in 2017 prior to initiating a Phase 1 clinical trial.

Recent Developments

Litigation Update

The class-action settlement we announced in December 2015 was completed on or about May 25, 2016 with the issuance of 1,561,578 shares of our common stock valued at \$4.5 million, or \$2.8817 a share, and payment of \$4 million in cash, of which \$3.5 million was paid by our insurance carriers and \$500,000 was paid out of company funds.

We announced in January 2016 the settlement of the California derivative claims pending against certain of our current or former directors and officers. The settlement, which is subject to preliminary court approval, notice to the company's stockholders and final court approval, calls for us to adopt certain corporate governance therapeutics and to issue to the plaintiffs' attorneys a total of \$700,000 of shares of our common stock valued at the market price of the common stock at the time (*i.e.*, average over 15 trading days), but not less than \$2.50 or more than \$3.75 per share. A hearing in the matter is scheduled for July 25, 2016.

Table of Contents

Liquidity

We had cash and cash equivalents of approximately \$55.9 million as of June 30, 2016, which includes the proceeds from a \$25 million debt financing earlier this year; the lenders have the option to accelerate and demand payment of all or any part of such amount in the event of a circumstance that could reasonably be expected to have a Material Adverse Effect (as defined in the loan and security agreement). As of the date of this prospectus supplement, the lender has not indicated any intention to accelerate or demand payment of the loan.

We believe our existing cash and cash equivalents, together with the net proceeds of this offering, will be sufficient to fund our operations for the foreseeable future.

Corporate Information

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

THE OFFERING

Common Stock offered by us	<p>_____ shares (excluding _____ shares of common stock issuable upon exercise of the warrants being offered in this offering). This prospectus supplement also relates to the offer and sale of the shares of common stock underlying the warrants being offered by us.</p>
Warrants offered by us	<p>Warrants to purchase up to _____ shares of our common stock. Each warrant is exercisable to purchase _____ of a share of our common stock at an exercise price of \$ _____ per whole share. The warrants will be exercisable upon issuance and will expire on the one-year anniversary of issuance. See Description of Our Securities.</p>
Common stock to be outstanding after this offering	<p>_____ shares assuming the warrants offered in this offering were to be immediately issued and exercised in full.</p>
Use of proceeds	<p>We intend to use the net proceeds of this offering for general corporate purposes, which may include working capital, capital expenditures, research and development and other commercial expenditures. See Use of Proceeds on page S-26 for further information.</p>
Risk factors	<p>See Risk Factors beginning on page S-12 of this prospectus supplement for a discussion of factors you</p>

should read and consider carefully before investing in our securities.

NASDAQ Capital Market symbol

CYTR

Except as otherwise indicated, all information in this prospectus supplement:

is based on 66,580,055 shares outstanding on March 31, 2016;

excludes 14,322,005 shares of our common stock subject to options outstanding as of March 31, 2016, having a weighted-average exercise price of \$3.05 per share;

excludes 5,881,177 shares of our common stock reserved for issuance under our stock option plan as of March 31, 2016;

excludes 8,359,618 shares of our common stock reserved for issuance upon exercise of outstanding warrants as of March 31, 2016, having a weighted-average exercise price of \$3.96 per share; and

shares of common stock issuable upon exercise of warrants to be issued in this offering.

On July 12, 2016, our stockholders approved an amendment to our stock option plan to increase the number of shares reserved for issuance under the plan by 10,000,000 shares.

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, 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 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 \$58.6 million and \$12.6 million for the year ended December 31, 2015 and the three months ended March 31, 2016, respectively. We had an accumulated deficit as of March 31, 2016 of \$377.7 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 security holders' 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 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, 2015, and we realized no revenue in the three months ended March 31, 2016. 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.

We had cash and cash equivalents of approximately \$55.9 million as of June 30, 2016, which includes the proceeds from a \$25 million debt financing earlier this year; the lenders have the option to accelerate and demand payment of all or any part of such amount in the event of a circumstance that could reasonably be expected to have a Material Adverse Effect (as defined in the loan and security agreement). As of the date of this prospectus supplement, the lender has not indicated any intention to accelerate or demand payment of the loan.

We believe that our existing cash and cash equivalents, together with the net proceeds of this offering, will be sufficient to fund our operations for the foreseeable future.

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 security holders 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;

S-10

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.

S-11

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

Table of Contents

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 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.

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.

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;

S-13

Table of Contents

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.

S-14

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, 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 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 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 our LADR technology platform, 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.

Table of Contents

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. 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 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 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 patents or 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 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.

Table of Contents

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.

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.

Table of Contents

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 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.

Table of Contents

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.

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 Eli Lilly's olaratumab currently in a Phase 3 clinical trial and Tracoon Pharmaceuticals TRC-105 in combination with pazopanib.

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 Tracoon 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 ipilimumab (Yervoy®) and SC16LD6.5 by Stem CentRx, Inc.

S-19

Table of Contents

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;

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 security holders a total of up to approximately \$18.3 million of future earnout merger consideration, subject to our achievement of specified net

Table of Contents

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 rely significantly on information technology and any failure, inadequacy, interruption or security lapse of that technology, including any cybersecurity incidents, could harm our ability to operate our business effectively.

We rely significantly on information technology and any failure, inadequacy, interruption or security lapse of that technology, including any cybersecurity incidents, could harm our ability to operate our business effectively. We maintain sensitive data pertaining to our Company on our computer networks, including information about our development activities, our intellectual property and other proprietary business information. Our internal computer systems and those of third parties with which we contract may be vulnerable to damage from cyber-attacks, computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures, despite the implementation of security measures. System failures, accidents or security breaches could cause interruptions to our operations, including material disruption of our development activities, result in significant data losses or theft of our intellectual property or proprietary business information, and could require substantial expenditures to remedy. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications or inappropriate disclosure of confidential or proprietary information, we could incur liability and our development programs could be delayed, any of which would harm our business and operations.

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 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

S-21

Table of Contents

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. In December 2015, we announced the selection of DK049 as the first new product candidate utilizing our LADR technology. 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 security holders 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 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 that you may pay for the shares of our common stock offered hereby. 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 that you may pay for the shares of our common stock offered hereby.

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 \$0.74 per share to a high of \$3.66 per share during the period January 1, 2016 through July 13, 2016, 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;

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.

S-23

Table of Contents

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, 2016, we had outstanding stock options to purchase 14,322,005 shares of our common stock at a weighted-average exercise price of \$3.05 per share and outstanding warrants to purchase 8,359,618 shares of common stock at a weighted-average exercise price of \$3.96 per share. 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 security holders.

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 cannot assure investors that we will be able to fully address the material weakness in our internal controls or that remediation efforts will prevent future material weaknesses.

We have identified a control deficiency in our financial reporting process concerning a non-routine and unusual item that constitutes a material weakness, for the year ended December 31, 2015. We have initiated certain measures, including performing a comprehensive review of significant and unusual transactions, to remediate this weakness, and plan to implement additional appropriate measures as part of this effort. There can be no assurance that we will be able to fully remediate our existing material weakness or that the comprehensive review of certain significant and unusual transactions will remediate or prevent these weaknesses from re-occurring in the future.

Further, there can be no assurance that we will not suffer from other material weaknesses in the future. If we fail to remediate these material weaknesses or fail to otherwise maintain effective internal controls over financial reporting in the future, such failure could result in a material misstatement of our annual or quarterly financial statements that would not be prevented or detected on a timely basis and which could cause investors and other users to lose confidence in our financial statements, limit our ability to raise capital and have a negative effect on the trading price of our common stock. Additionally, failure to remediate the material weaknesses or otherwise failing to maintain effective internal controls over financial reporting may also negatively impact our operating results and financial condition, impair our ability to timely file our periodic and other reports with the SEC, subject us to additional litigation and regulatory actions and cause us to incur substantial additional costs in future periods relating to the implementation of remedial measures.

We have been, and in the future may be, subject to legal or administrative actions that could adversely affect our results of operations and our business.

We announced in December 2015 and in January 2016 that we had agreed to settle federal securities class actions and stockholder derivative lawsuits filed in 2014 against us and certain of our officers and directors. Securities-related class action lawsuits and derivative litigation have often been brought against companies, including many biotechnology companies, which experience volatility in the market price of their securities. This risk is especially relevant for biotechnology and biopharmaceutical companies such as ours, which often experience significant stock price volatility in connection with their product development programs.

Although we carry director s and officer s and other liability insurance, the insurance may not be sufficient to cover future liabilities that we may incur in connection with possible legal or administrative actions.

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 security holders 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 security holders.

Table of Contents

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 security holders. 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 security holders 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 security holders 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 security holders. 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 security holders 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 security holders.

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 security holders, which could limit our security holders' 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 security holders, (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 security holders' 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 security holders. 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 security holders 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.

S-25

Table of Contents

Risks Associated With This Offering

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.

You will suffer substantial dilution. See **Dilution** in this prospectus supplement for more information of the dilution you will incur in this offering.

You may not be able to resell your warrants.

There is no established trading market for the warrants being offered in this offering, and we do not expect such a market to develop. In addition, we do not intend to apply for listing of the warrants on any securities exchange or other nationally recognized trading system, and you may not be able to resell your warrants. If your warrants cannot be resold, you will have to depend upon any appreciation in the value of our common stock over the exercise price of the warrants in order to realize a return on your investment in the warrants.

Investors will have no rights as a common stockholder with respect to their warrants until they exercise their warrants and acquire our common stock.

Until you acquire shares of our common stock upon exercise of your warrants, you will have no rights with respect to the shares of our common stock underlying such warrants except as set forth in the Warrants. Upon exercise of your warrants, you will be entitled to exercise the rights of a common stockholder only as to matters for which the record date occurs after the exercise date.

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.

USE OF PROCEEDS

We estimate that the net proceeds of this offering, after deducting the placement agent fees and expenses and the other estimated offering expenses payable by us, will be approximately \$.

We intend to use the net proceeds of this offering for general corporate purposes, which may include 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.

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.

CAPITALIZATION

The following table sets forth our cash and cash equivalents and capitalization as of March 31, 2016:

on an actual basis; and

on an as adjusted basis to give effect to the issuance of _____ units in this offering, at the public offering price of \$ _____ per unit, after deducting placement agent fees and expenses and the other estimated offering expenses payable by us excluding the proceeds, if any, from the exercise of warrants issued pursuant to this offering.

Table of Contents

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.

(unaudited) (in thousands, except share data)	AS OF MARCH 31, 2016	
	ACTUAL	AS ADJUSTED
Cash and cash equivalents	68,162,754	\$
Total assets	75,339,649	
Term loan, net-current	534,142	
Long-term Loan, net	22,911,337	
Total liabilities	41,761,197	
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; 66,580,065 shares issued and outstanding, actual; shares issued and outstanding, as adjusted	66,580	
Additional paid-in capital	411,249,758	
Accumulated deficit	(377,737,886)	
Total stockholders' equity	33,578,452	
Total liabilities and stockholders' equity	\$ 75,339,649	\$

DILUTION

Purchasers of units 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, 2016 was approximately \$0.50 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, 2016.

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 units in this offering (excluding shares of common stock issuable upon exercise of the warrants being offering in this offering) at a public offering price of \$ per unit, 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, 2016 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 unit	\$
Net tangible book value per share as of March 31, 2016	\$ 0.50
Increase per share attributable to this offering	\$
As adjusted net tangible book value per share as of March 31, 2016 after this offering	\$
Dilution per share to new investors participating in this offering	\$

The above table is based on 66,580,065 shares of common stock outstanding as of March 31, 2016, and excludes:

14,322,005 shares of our common stock subject to options outstanding as of March 31, 2016, having a weighted-average exercise price of \$3.05 per share;

5,881,177 shares of our common stock reserved for issuance in connection with future grants under our stock option plan as of March 31, 2016; and

8,359,618 shares of our common stock reserved for issuance upon exercise of outstanding warrants as of March 31, 2016, having a weighted-average exercise price of \$3.96 per share.

Table of Contents

On July 12, 2016, our stockholders approved an amendment to our stock option plan to increase the number of shares reserved for issuance under the plan by 10,000,000 shares.

To the extent that any options or warrants are exercised, new options are issued under our stock option 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.

DESCRIPTION OF OUR SECURITIES

We are offering _____ units, consisting of an aggregate of _____ shares of common stock and warrants to purchase an aggregate of _____ shares of common stock. Each unit consists of one share of common stock and a warrant to purchase _____ of a share of common stock at an exercise price of \$ _____ per whole share. The units will not be issued or certificated. The shares of common stock and the warrants are immediately separable and will be issued separately. This prospectus supplement also relates to the offering of the shares of common stock issuable upon exercise of the warrants being offered in this offering.

Common Stock

As of March 31, 2016, 66,580,065 shares of our common stock were issued and outstanding.

Each holder of our common stock is entitled to one vote for each share of common stock held on all matters submitted to a vote of stockholders. Common stockholders are not entitled to cumulative voting in the election of directors by our certificate of incorporation. This means that the holders of a majority of the shares voted will be able to elect all of the directors then standing for election. Subject to preferences that may apply to shares of preferred stock outstanding at the time, the holders of outstanding shares of our common stock are entitled to receive dividends out of assets legally available at the times and in the amounts that our board of directors may determine from time to time.

Upon our liquidation, dissolution or winding-up, the holders of our common stock will be entitled to share ratably in all assets remaining after payment of all liabilities and the liquidation preferences of any series of capital stock ranking senior to the common stock upon liquidation. Holders of common stock have no preemptive or conversion rights or other subscription rights. There are no redemption or sinking fund provisions applicable to the common stock. All outstanding shares of common stock are fully paid and non-assessable, and the shares of common stock to be issued under this prospectus supplement, when they are paid for, will be fully paid and non-assessable.

Our common stock is listed on The NASDAQ Capital Market under the symbol CYTR. The transfer agent of our common stock is American Stock Transfer & Trust Company, LLC.

Table of Contents

Warrants

Form. The warrants will be issued in certificated form.

Exercisability. The warrants will be exercisable upon issuance and will expire on the one-year anniversary of issuance. The warrants will be exercisable, at the option of each holder, in whole or in part by delivering to us a duly executed exercise notice and payment in full of the exercise price within three trading days in available funds for the number of shares of common stock purchased upon such exercise. If a registration statement registering the issuance or the resale of the shares of common stock underlying the warrants under the Securities Act is not effective or available, the holder may, in its sole discretion, elect to exercise the warrant through a cashless exercise, in which case the holder would receive upon such exercise the net number of shares of common stock determined according to the formula set forth in the warrant. No fractional shares of common stock will be issued in connection with the exercise of a warrant. In lieu of fractional shares, we will pay the holders an amount in cash equal to the fractional amount multiplied by the current market price of our common stock.

Exercise Limitation. A holder will not have the right to exercise any portion of the warrant if the holder (together with affiliates) would beneficially own in excess of 4.99% (or, at the election of a holder, 9.99%) of the number of shares of our common stock outstanding immediately after giving effect to the exercise, as such percentage of ownership is determined in accordance with the terms of the warrants. However, any holder may increase or decrease such percentage to any other percentage not in excess of 9.99% upon at least 61 days prior notice from the holder to us provided that any increase in the beneficiary ownership limitation shall not be effective until 61 days following notice from the holder to us.

Exercise Price. The exercise price per whole share of common stock purchasable upon exercise of the warrants is \$. The exercise price is subject to adjustment in the event of certain stock dividends and distributions, stock splits, stock combinations, reclassifications or similar events affecting our common stock.

Transferability. Subject to applicable laws, the warrants may be offered for sale, sold, transferred or assigned without our consent.

Table of Contents

Exchange Listing. The warrants will not be listed on The NASDAQ Capital Market or other securities exchange or nationally recognized trading system.

Fundamental Transactions. In the event of a fundamental transaction, as described in the warrants and generally including any merger or consolidation with or into another entity, as a result of which the holders of our outstanding voting securities as of immediately prior to such merger or consolidation hold less than a majority of the outstanding voting securities of the surviving or successor entity as of immediately after such merger or consolidation or a sale, transfer or other disposition of all or substantially all our property, assets or business to another person or entity, the holders of the warrants will be entitled to receive upon exercise of the warrants the kind and amount of securities, cash or other property that the holders would have received had they exercised the warrant immediately prior to such fundamental transactions.

Pro Rata Distributions. In the event that we distribute debt, securities, rights or warrants to purchase securities or other assets to holders of common stock, then upon exercise of the warrants, the holders will be entitled to receive the same distribution they would have received had they exercised the warrants immediately prior to the distribution.

Rights as a Stockholder. Except as otherwise provided in the warrants or by virtue of such holders' ownership of shares of our common stock, the holder of a warrant does not have the rights or privileges of a holder of our common stock, including any voting rights, until the holder exercises the warrant except as set forth in warrant.

Table of Contents**PLAN OF DISTRIBUTION**

We are offering _____ units. However, there is no minimum offering amount required as a condition to closing and we may sell significantly fewer units in the offering. The offering will terminate on July _____, 2016, unless the offering is fully subscribed before that date or we decide to terminate the offering prior to that date.

In determining the offering price of the units, we will consider a number of factors including, but not limited to, the current market price of our common stock, trading prices of our common stock over time, the illiquidity and volatility of our common stock, our current financial condition and the prospects for our future cash flows and earnings, and market and economic conditions at the time of the offering. Once the offering price is determined, the offering price for the units will remain fixed for the duration of the offering.

H.C. Wainwright & Co., LLC (the Placement Agent) has agreed to act as our exclusive placement agent in connection with the offering pursuant to the terms and conditions of an engagement agreement. The Placement Agent is not purchasing or selling any securities offered by this prospectus, and is not required to arrange for the purchaser or sale of any specific number or dollar amount of securities, but will use its reasonable best efforts to arrange for the sale of the securities offered by this prospectus. We have entered into a securities purchase agreement directly with certain institutional investors which will purchase not less than \$ _____ of units in this offering. We will not enter into any securities purchase agreement with investors which will purchase less than \$ _____ of units in this offering and such investors which purchase less than \$ _____ shall rely solely on this prospectus in connection with the purchase of securities in this offering. The Placement Agent may retain one or more sub-agents or selected dealers in connection with the offering.

We have agreed to pay to the Placement Agent a placement agent fee equal to six percent (6%) of the aggregate gross proceeds to us from the sale of the securities in the offering. In addition, we have agreed to pay the placement agent a management fee equal to 1% of the gross proceeds of this offering and to reimburse the placement agent for offering expenses in the non-accountable sum of \$25,000 and for legal fees and expenses in the non-accountable sum of \$100,000, subject to compliance with FINRA Rule 5110(f)(2)(D)(i). In addition, we have agreed to pay the placement agent a cash fee equal to 6% of the gross proceeds received by us upon the exercise of any warrants issued in this offering, if any. We estimate total expenses of this offering, excluding the placement agent fees, will be approximately \$ _____. The following table shows the per share and total fees we will pay to the placement agent assuming the sale of all of the shares offered pursuant to this prospectus.

Per unit	\$
Total	\$

Table of Contents

In addition, we have granted to the Placement Agent a right to act as joint lead manager with respect to additional raises of funds by means of a public offering or private placement of equity or debt securities using an underwriter or placement agent or financing any indebtedness using an agent or manager during the 12 months following the consummation of this offering, subject to FINRA Rule 5110(f)(2)(D)(ii).

The engagement agreement provides that we will indemnify the Placement Agent against specified liabilities, including liabilities under the Securities Act of 1933, as amended. The Placement Agent may be deemed to be an underwriter within the meaning of Section 2(a)(11) of the Securities Act, and any commissions received by it and any profit realized on the resale of the securities sold by it while acting as principal might be deemed to be underwriting discounts or commissions under the Securities Act. As an underwriter, the Placement Agent would be required to comply with the Securities Act and the Securities Exchange Act of 1934, as amended (Exchange Act), including without limitation, Rule 10b-5 and Regulation M under the Exchange Act. These rules and regulations may limit the timing of purchases and sales of shares of common stock, over-allotment purchase rights and warrants by the Placement Agent acting as principal. Under these rules and regulations, the Placement Agent:

may not engage in any stabilization activity in connection with our securities; and

may not bid for or purchase any of our securities or attempt to induce any person to purchase any of our securities, other than as permitted under the Exchange Act, until it has completed its participation in the distribution.

Table of Contents

LEGAL MATTERS

The validity of the securities 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 placement agent by Ellenoff Grossman & Schole LLP, New York, New York.

EXPERTS

The financial statements and schedule as of December 31, 2015 and 2014 and for each of the three years in the period ended December 31, 2015 and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2015 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 (the report on the effectiveness of internal control over financial reporting expresses an adverse opinion on the effectiveness of the company's internal control over financial reporting as of December 31, 2015), incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

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.

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, 2015 filed with the SEC on March 11, 2016;

Table of Contents

our Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2016, filed with the SEC on May 10, 2016;

our Current Reports on Form 8-K filed with the SEC on January 6, 2016, January 7, 2016, January 11, 2016, February 9, 2016, February 11, 2016, March 11, 2016, May 11, 2016, May 27, 2016, June 1, 2016, June 7, 2016 and July 14, 2016, 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 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

\$171,221,250

We may offer and sell from time to time up to \$171,221,250 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 June 7, 2016, the last sale price of our common stock as reported on The NASDAQ Capital Market was \$2.56.

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 12 of 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 June 17, 2016

Table of Contents

TABLE OF CONTENTS

	Page
<u>ABOUT THIS PROSPECTUS</u>	2
<u>NOTE ON FORWARD-LOOKING STATEMENTS</u>	2
<u>INDUSTRY DATA</u>	2
<u>TRADEMARKS</u>	3
<u>ABOUT CYTRX</u>	3
<u>RISK FACTORS</u>	12
<u>USE OF PROCEEDS</u>	12
<u>FINANCIAL RATIOS</u>	12
<u>DIVIDEND POLICY</u>	13
<u>THE SECURITIES THAT WE MAY OFFER</u>	13
<u>DESCRIPTION OF CAPITAL STOCK</u>	13
<u>DESCRIPTION OF WARRANTS</u>	16
<u>DESCRIPTION OF UNITS</u>	17
<u>PLAN OF DISTRIBUTION</u>	18
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	19
<u>INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE</u>	19
<u>LEGAL MATTERS</u>	20
<u>EXPERTS</u>	20

Table of Contents

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement (Reg. No. 333-208803) 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 More 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.

NOTE ON FORWARD-LOOKING STATEMENTS

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

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 referred to under "Risk Factors" on page 12 of this prospectus. These and other factors could cause our future performance to differ materially from our assumptions and estimates.

Table of Contents

TRADEMARKS

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

ABOUT CYTRX

Company Overview

CytRx Corporation (we, us, our or the company) is 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 have reported positive top-line efficacy results (median progression-free survival, progression-free survival 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 the likelihood that the study endpoint (in this case tumor progression) will be reached during a given period are an important measure of the reliability and uniformity of the absolute data for progression-free survival, or PFS. The trial investigated the efficacy and safety of aldoxorubicin compared with doxorubicin in subjects with first-line metastatic, locally advanced or unresectable STS. Aldoxorubicin combines the chemotherapeutic agent doxorubicin with a novel linker-molecule that binds specifically to albumin in the blood to allow for delivery of higher amounts of doxorubicin (3 1/2 to 4 times) without the major dose-limiting toxicities seen with 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, and we have received approval from the FDA to continue dosing patients with aldoxorubicin until disease progression in that clinical trial. The Phase 3 trial is being conducted under a Special Protocol Assessment, or SPA, granted by the U.S. Food and Drug Administration, or FDA. The SPA means that the FDA agrees that the design and analyses proposed in the Phase 3 trial protocol are acceptable to support regulatory approval of the product candidate with respect to effectiveness of the indication studied, and will not subsequently change its perspective on these matters, unless previously unrecognized public or animal health concerns were to arise or we were to subsequently modify the protocol. Thus, if the study demonstrates an acceptable benefit-risk profile as determined by the FDA, it would suffice as the single pivotal trial to demonstrate effectiveness and would support registration of aldoxorubicin for this indication. The clinical trial has completed its target enrollment of 400 patients at approximately 79 clinical sites in the U.S., Europe, Canada, Latin America and Australia. We expect to report the top-line results on PFS the trial s primary endpoint, **[by mid-July] 2016.**

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 trial in combination with ifosfamide in patients with soft tissue sarcoma, and a Phase 1b trial in combination with gemcitabine in subjects with metastatic solid tumors. We have completed a global Phase 2b clinical trial with aldoxorubicin as a first-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.

In addition to aldoxorubicin, we are currently completing pre-clinical development for DK049, a novel anti-cancer drug conjugate that utilizes our Linker Activated Drug Release (LADRTM) technology. DK049 was created at our

laboratory facility in Freiburg, Germany, and employs a proprietary linker that is both pH sensitive and requires a specific enzyme for the release of the cytotoxic payload. DK049 has demonstrated significant anti-tumor activity in multiple animal models implanted with human tumors, including non-small cell lung, ovarian and pancreatic cancers. We anticipate filing an Investigational New Drug Application (IND) in the second half of 2016 prior to initiating a Phase 1 clinical trial.

We plan to expand our pipeline of oncology candidates utilizing our LADRTM technology by creating both albumin-binding drug conjugates and antibody-drug conjugates. This technology allows for targeting to the tumor either by albumin or antibodies and can deliver anti-cancer agents that are 10-1000 times more potent than traditional chemotherapies.

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.

Table of Contents

Technology	Product candidate	Indication(s)	Stage of Development
Doxorubicin conjugate	Aldoxorubicin	Soft Tissue Sarcoma	Pivotal Global Phase 3 ongoing
		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
LADR™	DK049	To be announced	Pre-clinical
LADR™ for albumin-binding drug conjugates	To be announced	To be announced	Pre-clinical
LADR™ for antibody-drug conjugates	To be announced	To be announced	Pre-clinical

Our Clinical Development Programs

Our current clinical development programs are discussed below.

Aldoxorubicin

Aldoxorubicin is a conjugate of the commonly prescribed chemotherapeutic agent doxorubicin that binds to circulating albumin in the bloodstream and is believed to concentrate the drug 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, we initiated under an SPA granted by the FDA 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 certain 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 doxorubicin is taken up by the tumor, the acidic environment within the tumor and in the cancer cells themselves causes cleavage of the acid-sensitive linker; and

free doxorubicin is then released in the tumor.

Pre-clinical data

In a variety of preclinical models, aldorubicin was superior to doxorubicin at equitoxic doses in its ability to allow an increase in the total doxorubicin dose, its antitumor efficacy and its safety, including a reduction in cardiotoxicity. Animal studies conducted by aldorubicin 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 have also announced additional data from a study of aldorubicin in immunodeficient mice transplanted with human glioblastoma cells in their brain that showed those animals treated with aldorubicin had a median survival rate of more than 63 days,

Table of Contents

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 aldorubicin-treated animals, while doxorubicin did not appear to enter the tumor or brain to any significant degree and showed little or no efficacy in the progression of these brain tumors. Aldorubicin 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 aldorubicin 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 *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 aldorubicin in patients with advanced solid tumors who had either relapsed or failed to respond to their prior chemotherapy and presented favorable data at the American Society for Clinical Oncology Meeting in June 2012. In that Phase 1b/2 clinical trial, clinical benefit (defined as partial response or stable disease of more than four months) was shown in ten of 13 (76.9%) evaluable patients with relapsed or refractory STS. The median number of cycles of aldorubicin administered at the maximum tolerable dose was eight. The results of this clinical trial were published in February 2015 in the peer-reviewed journal *Cancer* (*Cancer*, 2015 Feb 15; 121(4); 570-9).

In addition, best responses for the 13 evaluable STS trial subjects included the following: five (38.5%) achieved partial response, as defined as shrinkage of target tumors of more than 30%; six (46%) 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 aldorubicin 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. Final observed median PFS for advanced STS patients in the trial was 11.25 months, and median overall survival was 21.71 months (Publication in *Cancer*, 2015 Feb 15). In addition, following 8 cycles of aldorubicin, two patients experienced no progression of disease for 23 and 15 months, respectively, despite no further treatment.

In connection with our Phase 1b pharmacokinetics clinical trial evaluating the pharmacokinetics and safety of aldorubicin in patients with metastatic solid tumors who have either relapsed or not responded to treatment with standard therapies, we announced data demonstrating that aldorubicin 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 aldorubicin from doxorubicin, which has a distribution half-life of about five minutes according to its package insert. Complete details from this Phase 1b trial were published online in the journal *Investigational New Drugs* in November 2014 (Publication in *Invest New Drugs*, 2015 Apr 15; 33(2):341-8).

We completed our global Phase 2b clinical trial to evaluate the preliminary efficacy and safety of aldorubicin as a first-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 aldorubicin and native doxorubicin, which is dose-limited due to toxicity, as a first-line therapy.

The Phase 2b clinical trial with aldoxorubicin in patients with STS was an international trial in 31 treatment centers under the direction of Sant P. Chawla, M.D., F.R.A.C.P., Director of the Sarcoma Oncology Center in Santa Monica, California. The Phase 2b clinical trial's primary objectives 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, and overall survival. The results from this trial were published in the Journal of the American Medical Association (JAMA) Oncology in September 2015 (JAMA Oncol. 2015 Sep 17:1-9.).

Table of Contents

The central radiology review, as well as the investigators' own assessments, showed an 80% to 100% improvement in PFS among patients treated with aldorubicin. In an intent-to-treat analysis, the investigator-assessed median PFS was 8.3 months for aldorubicin patients versus 4.6 months for doxorubicin patients ($p=0.0006$), while the blinded central radiology review indicated that median PFS for aldorubicin patients was 5.6 months versus 2.7 months for doxorubicin patients ($p=0.0228$). Per investigators, 68.1% of aldorubicin patients had not progressed at six months, compared with 33.0% of doxorubicin-treated patients ($p=0.008$). By blinded central radiology review, 45.7% of aldorubicin patients had not progressed at six months, compared with 22.9% of doxorubicin patients ($p=0.02$).

The overall response rate as determined by the investigators was 22.9% for aldorubicin subjects (2.0% complete response and 21.3% 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 aldorubicin subjects had a partial response while none of the doxorubicin subjects exhibited any objective response.

Additional analysis determined hazard ratios for the primary endpoint of PFS by both investigators at study sites and by the blinded radiology review. The hazard ratio for investigator-read scans is 0.37 (95% confidence interval, range of 0.212 to 0.643) ($p=0.0004$), reflecting a 63% reduction in the risk of disease progression for patients treated with aldorubicin; and the hazard ratio for central lab scans is 0.586 (95% confidence interval, range of 0.358 to 0.960) ($p=0.034$), reflecting a 41% reduction in the risk of disease progression for the aldorubicin-treated patients. Hazard ratios are an important measure of the reliability and uniformity of the data for PFS, and where the upper limit is less than one 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 analysis describes the time it takes for tumors to progress in individual patients, showed significant improvement in subjects treated with aldorubicin versus subjects treated with doxorubicin.

The overall survival results from the clinical trial demonstrated a 27 percent reduction in the risk of death compared to patients treated with doxorubicin (HR 0.73: 95% confidence interval 0.44-1.20), the current standard-of-care in this indication. In addition, aldorubicin-treated patients demonstrated a 41% likelihood of surviving more than 2 years, a 2-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 aldorubicin-treated patients versus 14.3 months (95% confidence interval 8.6-20.6) for doxorubicin treated patients ($p=0.21$). For treatment-naïve patients, representing 90% of the patients in the clinical trial, median overall survival was 15.8 months (95% confidence interval 13.0-not reached) for aldorubicin-treated patients versus 13.8 months (95% confidence interval 8.6-19.8) for doxorubicin treated patients ($p=0.14$).

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

In the first quarter of 2014, we initiated a pivotal global Phase 3 clinical trial to evaluate the efficacy and safety of aldorubicin as a second-line treatment for patients with STS under a Special Protocol Assessment with the FDA. This multicenter, randomized, open-label Phase 3 clinical trial is designed to enroll approximately 400 patients with metastatic, locally advanced or unresectable soft tissue sarcomas 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 aldorubicin 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 progression-free survival (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 doxorubicin until disease progression (defined as an increase in the size of measurable tumors by 20% or the development of a new tumor lesion), which creates the potential for substantially improved Phase 3 efficacy results.

Following discussions with the FDA, the Phase 3 protocol was agreed upon under a Special Protocol Assessment (SPA). As part of that assessment, the FDA agreed that, barring unrecognized public or human health concerns, the design and planned analysis of the study adequately addresses the objectives necessary to support a regulatory submission for approval.

Table of Contents

The clinical trial has completed its target enrollment of 400 patients at approximately 79 clinical sites in the U.S., Europe, Canada, Latin America and Australia. CytRx expects to report the top-line results on progression-free survival, the trial's primary endpoint, in the first half of 2016.

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 (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 OS, 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 U.S., Spain 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 has enrolled its target of 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 U.S. 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 a Phase 1b trial in combination with ifosfamide in patients with STS, and a Phase 1b trial in combination with gemcitabine in subjects with metastatic solid tumors. Since most 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 treat patients with sarcomas, pancreatic cancer, ovarian cancer and lung cancer.

Drug Discovery Laboratory

Our laboratory, located in Freiburg, Germany, is conducting discovery and translational research to create drug candidates that utilize our LADR technologies to couple cytotoxic agents and proteins either inside the body or externally, and then concentrate 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 and using LADR linkers to create unique antibody-drug conjugates. We recently announced the development of DK049, a novel anti-cancer drug conjugate that utilizes our LADR technology, and anticipate filing an IND for DK049 in the second half of 2016 prior to initiating a Phase 1 clinical trial.

Disposition of Molecular Chaperone Assets

Until 2011, we owned the rights to two drug candidates, arimoclomol and iroxoanadine, based on molecular chaperone regulation technology that were designed to repair or degrade mis-folded proteins associated with disease. On May 13, 2011, we sold all pre-clinical and clinical data, intellectual property rights and other assets relating to those compounds to Orphazyme ApS in exchange for a cash payment of \$150,000 and the right to receive various future payments that are contingent upon the achievement of specified regulatory and business milestones, as well as royalty

payments based on a specified percentage of any eventual net sales of products derived from the assets.

Innovive Acquisition Agreement

On September 19, 2008, we completed our merger acquisition of Innovive Pharmaceuticals, Inc., or Innovive, and its clinical-stage cancer product candidates, including aldoxorubicin and tamibarotene. Under the merger agreement by which we acquired Innovive, we agreed to pay the former Innovive stockholders 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. The earnout will be accrued if and when earned.

Table of Contents

Research and Development

Expenditures for research and development activities related to continuing operations were \$43.4 million and \$36.7 million for the years ended December 31, 2015 and 2014, respectively, and \$8.2 million for the three months ended March 31, 2016, or approximately 68%, 74% and 67%, respectively, of our total expenses.

Manufacturing

We do not have the facilities or expertise to manufacture clinical supplies of doxorubicin or any of our other product candidates, and we lack the resources and capability to manufacture any of our product candidates on a commercial scale. Accordingly, we are dependent upon third-party manufactures, 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 doxorubicin. In September, 2015, we entered into an agreement with a supplier to purchase doxorubicin hydrochloride both on a clinical as well as a commercial scale. However, we currently have no other supply arrangements for the commercial manufacture of doxorubicin or any manufacturing supply arrangements for any other potential product candidates, and we may not be able to secure needed supply arrangements on attractive terms, or at all. Our failure to secure these arrangements as needed could have a material adverse effect on our ability to complete the development of our products or to commercialize them.

Commercialization and Marketing

We recently hired Olivia Ware as our Chief Commercial Officer and have initiated activities to build our sales, marketing and commercial product distribution capabilities in preparation for the US launch of doxorubicin. If doxorubicin is approved, we expect to commercialize it in the U.S. with a small internal commercial group and an outsourced specialty field sales force.

We intend to commercialize doxorubicin outside the US starting in the EU-5 countries. Our commercial strategy may include the use of strategic partners, distributors, a contract sales force or the establishment of our own sales force. We plan to further evaluate these alternatives as we approach approval for doxorubicin.

As additional product candidates advance through our pipeline, our commercial plans may change. In particular, some of our pipeline assets target potentially large solid tumor indications. Factors such as clinical data, the size of the development programs, the size of the target market, the size of a commercial infrastructure, and manufacturing needs may influence our strategies in the U.S., the European Union, and other territories.

Patents and Proprietary Technology

We actively seek patent protection for our technologies, processes, uses, and ongoing improvements and consider our patents and other intellectual property to be critical to our business. We regularly evaluate the patentability of new inventions and improvements developed by us or our collaborators, and, whenever appropriate, will endeavor to file U.S. and international patent applications to protect these new inventions and improvements. We cannot be certain that any of the current pending patent applications we have filed or licensed, or any new patent applications we may file or license, will ever be issued in the U.S. or any other country. There also is no assurance that any issued patents will be effective to prevent others from using our products or processes. It is also possible that any patents issued to us, as well as those we have licensed or may license in the future, may be held invalid or unenforceable by a court, or third parties could obtain patents that we would need to either license or to design around, which we may be unable to do. Current and future competitors may have licensed or filed patent applications or received patents, and may acquire additional patents and proprietary rights relating to compounds, products or processes that may be competitive with

ours.

In addition to patent protection, we attempt to protect our proprietary products, processes and other information by relying on trade secrets and non-disclosure agreements with our employees, consultants and certain other persons who have access to such products, processes and information. Under the agreements, all inventions conceived by employees are our exclusive property, but there is no assurance that these agreements will afford significant protection against misappropriation or unauthorized disclosure of our trade secrets and confidential information.

As of December 31, 2015, we held rights in four granted U.S. patents, 55 granted foreign patents, three pending U.S. applications, and twenty-two pending foreign patent applications covering aldorubicin and related technologies. Our intellectual property holdings relating to aldorubicin and related technologies include an exclusive license from KTB Tumorforschungs GmbH, or KTB, to U.S. and foreign patents and patent applications. Patents and applications that cover pharmaceutical compositions of aldorubicin, processes for their production, and their use in treatment methods (e.g., cancer (including glioblastoma), viral diseases, autoimmune diseases, and acute or chronic inflammatory diseases) have unextended patent terms expiring between June 2020 and June 2034. Additionally, we have three pending U.S. provisional patent applications covering our LADR technology and DK049.

Table of Contents

License Agreements

Aldoxorubicin

We have an agreement with KTB for the license of patent rights held by KTB for the worldwide development and commercialization of aldoxorubicin. The license is exclusive and applies to all products that may be subject to the licensed intellectual property in all fields of use. We may sublicense the intellectual property in our sole discretion. Pursuant to an amendment to the license agreement entered into in March 2014, we also have a non-exclusive worldwide license to any additional technology that is claimed or disclosed in the licensed patents and patent applications for use in the field of oncology.

Under the agreement, we must make payments to KTB in the aggregate of up to \$7.5 million upon meeting clinical and regulatory milestones, and up to and including the product's second final marketing approval. We also agreed 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 million for each additional final marketing approval that we obtain.

Pursuant to the March 2014 license amendment, we agreed to make a \$500,000 milestone payment upon first dosing of a patient in a first phase I clinical trial for each product using the additional technology. In the event that by February 28, 2017, no such payment has become due, we have agreed to pay KTB \$500,000, which payment can be made, in our discretion, in cash or in shares of our common stock. If we elect to make the payment in shares of common stock, our shares will be valued at the volume-weighted average price (VWAP) over the preceding 60 trading days, to be calculated on February 28, 2017.

In the event that we must pay a third party in order to exercise our rights to the intellectual property under the agreement, we are entitled to deduct a percentage of those payments from the royalties due KTB, up to an agreed upon cap.

Under the agreement with KTB, we must use commercially reasonable efforts to conduct the research and development activities we determine are necessary to obtain regulatory approval to market aldoxorubicin in those countries that we determine are commercially feasible. Under the agreement, KTB is to use its commercially reasonable efforts to provide us with access to suppliers of the active pharmaceutical ingredient, or API, of aldoxorubicin, on the same terms and conditions as may be provided to KTB by those suppliers.

The agreement will expire on a product-by-product basis upon the expiration of the subject patent rights. We have the right to terminate the agreement on 30 days' notice, provided we pay a cash penalty to KTB. KTB may terminate the agreement if we are in breach and the breach is not cured within a specified cure period, or if we fail to use diligent and commercial efforts to meet specified clinical milestones.

Competition

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.

STS patients are typically treated with surgery followed by radiation therapy. For patients ineligible for surgery, radiation or both, chemotherapy 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. In October 2015, the Janssen unit of Johnson & Johnson received approval for trabectedin (Yondelis[®]) for the treatment of patients with leiomyosarcoma and liposarcoma, that have previously received an anthracycline and ifosfamide or an anthracycline followed by another chemotherapy. In January 2016,

Table of Contents

the FDA approved Eisai's eribulin (Halaven®) as a treatment for patients with unresectable or metastatic liposarcoma who have received a prior anthracycline. Eli Lilly is conducting a Phase 3 clinical trial with olaratumab in combination with doxorubicin in first-line STS. Eli Lilly stated in October 2015 that they plan to submit a rolling new drug application based on the Phase 2 clinical trial results in STS. There are other approaches to treating STS in clinical development, including Morphotek's ontuxizumab in combination with chemotherapy, and Traccon Pharmaceuticals' TRC-105 in combination with pazopanib.

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 nivolumab by Bristol-Myers Squibb, DCVax by Northwest Biotherapeutics, DelMar Pharmaceuticals' VAL-083, TRC-105 from Traccon 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 nivolumab (Opdivo®) and ipilimumab (Yervoy®) and SC16LD6.5 by Stem CentRx, Inc.

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

Government Regulation

The U.S. and other developed countries extensively regulate the preclinical and clinical testing, manufacturing, labeling, storage, record-keeping, advertising, promotion, export, marketing and distribution of drugs and biologic products. The FDA, under the Federal Food, Drug, and Cosmetic Act, the Public Health Service Act and other federal statutes and regulations, regulates pharmaceutical and biologic products.

To obtain approval of our product candidates from the FDA, we must, among other requirements, submit data supporting safety and efficacy for the intended indication as well as detailed information on the manufacture and composition of the product candidate. In most cases, this will require extensive laboratory tests and preclinical and clinical trials. The collection of these data, as well as the preparation of applications for review by the FDA involve significant time and expense. The FDA also may require post-marketing testing to monitor the safety and efficacy of approved products or place conditions on any approvals that could restrict the therapeutic claims and commercial applications of these products. Regulatory authorities may withdraw product approvals if we fail to comply with regulatory standards or if we encounter problems at any time following initial marketing of our products.

The first stage of the FDA approval process for a new drug involves completion of preclinical studies and the submission of the results of these studies to the FDA. These data, together with proposed clinical protocols, manufacturing information, analytical data and other information submitted to the FDA, in an investigational new drug application, or IND, must become effective before human clinical trials may commence. Preclinical studies generally involve FDA regulated laboratory evaluation of product characteristics and animal studies to assess the efficacy and safety of the product candidate.

After the IND becomes effective, a company may commence human clinical trials. These are typically conducted in three sequential phases, but the phases may overlap. Phase 1 trials consist of testing of the product candidate in a small number of patients

Table of Contents

or healthy volunteers, primarily for safety at one or more doses. Phase 2 trials, in addition to safety, evaluate the efficacy of the product candidate in a patient population somewhat larger than Phase 1 trials. Phase 3 trials typically involve additional testing for safety and clinical efficacy in an expanded population at multiple test sites. A company must submit to the FDA a clinical protocol, accompanied by the approval of the Institutional Review Boards at the institutions participating in the trial, prior to commencement of each clinical trial.

To obtain FDA marketing authorization, a company must submit to the FDA the results of the preclinical and clinical testing, together with, among other things, detailed information on the manufacture and composition of the product candidate, in the form of a new drug application, or NDA.

The amount of time taken by the FDA for approval of an NDA will depend upon a number of factors, including whether the product candidate has received priority review, the quality of the submission and studies presented, the potential contribution that the compound will make in improving the treatment of the disease in question, and the workload at the FDA.

The FDA may, in some cases, confer upon an investigational product the status of a fast-track product. A fast-track product is defined as a new drug or biologic intended for the treatment of a serious or life-threatening condition that demonstrates the potential to address unmet medical needs for this condition. The FDA can base approval of an NDA for a fast-track product on an effect on a surrogate endpoint, or on another endpoint that is reasonably likely to predict clinical benefit. If a preliminary review of clinical data suggests that a fast-track product may be effective, the FDA may initiate review of entire sections of a marketing application for a fast-track product before the sponsor completes the application.

We anticipate that our products will be manufactured by our strategic partners, licensees or other third parties. Before approving an NDA, the FDA will inspect the facilities at which the product is manufactured and will not approve the product unless the manufacturing facilities are in compliance with the FDA's cGMP, which are regulations that govern the manufacture, holding and distribution of a product. Our manufacturers also will be subject to regulation under the Occupational Safety and Health Act, the National Environmental Policy Act, the Nuclear Energy and Radiation Control Act, the Toxic Substance Control Act and the Resource Conservation and Recovery Act. Following approval, the FDA periodically inspects drug and biologic manufacturing facilities to ensure continued compliance with the good manufacturing practices regulations. Our manufacturers will have to continue to comply with those requirements. Failure to comply with these requirements subjects the manufacturer to possible legal or regulatory action, such as suspension of manufacturing or recall or seizure of product. Adverse patient experiences with the product must be reported to the FDA and could result in the imposition of marketing restrictions through labeling changes or market removal. Product approvals may be withdrawn if compliance with regulatory requirements is not maintained or if problems concerning safety or efficacy of the product occur following approval.

The labeling, advertising, promotion, marketing and distribution of a drug or biologic product also must be in compliance with FDA and Federal Trade Commission requirements which include, among others, standards and regulations for off-label promotion, industry sponsored scientific and educational activities, promotional activities involving the internet, and direct-to-consumer advertising. We also will be subject to a variety of federal, state and local regulations relating to the use, handling, storage and disposal of hazardous materials, including chemicals and radioactive and biological materials. In addition, we will be subject to various laws and regulations governing laboratory practices and the experimental use of animals. In each of these areas, as above, the FDA has broad regulatory and enforcement powers, including the ability to levy fines and civil penalties, suspend or delay issuance of product approvals, seize or recall products, and deny or withdraw approvals.

We will also be subject to a variety of regulations governing clinical trials and sales of our products outside the U.S. Whether or not FDA approval has been obtained, approval of a product candidate by the comparable regulatory authorities of foreign countries and regions must be obtained prior to the commencement of marketing the product in those countries. The approval process varies from one regulatory authority to another and the time may be longer or shorter than that required for FDA approval. In the European Union, Canada and Australia, regulatory requirements and approval processes are similar, in principle, to those in the U.S.

Employees

As of June 1, 2016, we had 29 employees, ten of whom were engaged in clinical development activities, nine of whom were engaged in preclinical research at our Freiburg, Germany laboratory, and ten of whom were involved in management and administrative operations.

Table of Contents**Corporate Information**

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

RISK FACTORS

Investing in our securities involves significant risks. The prospectus supplement relating to a particular offering will contain a discussion of risks applicable to an investment in the securities offered. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed under the heading Risk Factors in the applicable prospectus supplement together with all of the other information contained in the prospectus supplement or appearing or incorporated by reference in this prospectus.

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 pre-commercialization and, subject to regulatory approval, commercialization activities for aldoxorubicin and for other working capital and general corporate purposes, including the clinical trials of our product candidates. General corporate purposes also may include funding of capital expenditures, payments in connection with possible future acquisitions and strategic investments and repayment of future indebtedness.

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.

FINANCIAL RATIOS

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

	Year Ended December 31					Three Months Ended
	2011	2012	2013	2014	2015	March 31, 2016
Ratio of earnings to combined fixed charges and preference dividends						
Deficiency of earnings available to cover fixed charges and preferred dividends	(a)	(b)	(c)	(d)	(e)	(f)

(a) Earnings in the fiscal year ended December 31, 2011 were inadequate to cover combined fixed charges and preference dividends. The coverage deficiency was approximately \$14.2 million.

- (b) Earnings in the fiscal year ended December 31, 2012 were inadequate to cover combined fixed charges and preference dividends. The coverage deficiency was approximately \$17.9 million.
- (c) Earnings in the fiscal year ended December 31, 2013 were inadequate to cover combined fixed charges and preference dividends. The coverage deficiency was approximately \$47.2 million.
- (d) Earnings in the fiscal year ended December 31, 2014 were inadequate to cover combined fixed charges and preference dividends. The coverage deficiency was approximately \$30.0 million.
- (e) Earnings in the year ended December 31, 2015 were inadequate to cover combined fixed charges and preference dividends. The coverage deficiency was approximately \$58.6 million.
- (f) Earnings in the three months ended March 31, 2016 were inadequate to cover combined fixed charges and preference dividends. The coverage deficiency was approximately \$12.6 million.

The ratio is computed by dividing earnings by combined fixed charges and preference dividends. For this purpose, earnings are calculated as follows: (i) adding (a) net income (loss) from continuing operations before adjustment for any income or loss from any equity investees; (b) fixed charges; (c) amortization of any capitalized interest; (d) any distributed income of any equity investees; and (e) our share of any pre-tax losses of any equity investees for which charges arising from guarantees are included in fixed charges; and (ii) subtracting from such sum (a) any interest capitalized; (b) any preferred security dividend requirements of any consolidated subsidiaries; and (c) any non-controlling interest in the pre-tax income (loss) of any subsidiaries that have not incurred fixed charges. Equity investees, if any, are investments that we account for using the equity method of accounting.

Table of Contents

Fixed charges consist of that portion of rental expense associated with certain facility and equipment leases considered to be a reasonable estimate of the interest factor. We did not pay or accrue any preference dividends for the periods presented.

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.

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 \$171,221,250 in the aggregate of:

shares of our common stock, par value \$0.001 per share;

shares of our preferred stock, par value \$0.01 per share;

warrants to purchase our common stock or preferred stock; and

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

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

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

DESCRIPTION OF CAPITAL STOCK

As of March 31, 2016, our authorized capital stock consisted of 250,000,000 shares of common stock, \$0.001 par value per share, of which 66,580,065 shares were outstanding, and 5,000,000 shares of preferred stock, \$0.01 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. Holders of our common stock have no preemptive, conversion or subscription rights, and there are no redemption or sinking fund provisions with respect to our common stock.

Table of Contents

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;

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;

Table of Contents

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

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

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

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

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

Anti-Takeover Measures

Delaware Law

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

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

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

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

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

various business combinations with a corporation for a three-year period, although the stockholders may elect not to be governed by this section, by adopting an amendment to the certificate of incorporation or by-laws, effective 12 months after adoption. Our amended and restated certificate of incorporation and by-laws do not opt 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;

Table of Contents

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.

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.

Table of Contents

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.

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;

Table of Contents

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

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

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

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

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

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

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

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

PLAN OF DISTRIBUTION

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 reallocated or paid to dealers.

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

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

at market prices prevailing at the time of sale;

at prices related to such prevailing market prices; or

at negotiated prices.

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

Table of Contents

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.

WHERE YOU CAN FIND MORE INFORMATION

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

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

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

Edgar Filing: CYTRX CORP - Form 424B2

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, 2015 filed with the SEC on March 11, 2016;

our Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2016, filed with the SEC on May 10, 2016;

Table of Contents

our Current Reports on Form 8-K filed with the SEC on January 6, 2016, January 7, 2016, January 11, 2016, February 9, 2016, February 11, 2016, March 11, 2016, May 11, 2016, May 27, 2016, June 1, 2016 and June 7, 2016, 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 by us pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date on which we filed the registration statement of which this prospectus is a part and prior to the termination of this offering (excluding those portions of any Form 8-K that are not deemed filed pursuant to the General Instructions of Form 8-K).

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

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

LEGAL MATTERS

The validity of the securities being offered hereby has been passed upon for us by TroyGould PC, Los Angeles, California. TroyGould PC and some of its attorneys own shares of our common stock constituting in the aggregate less than 1% of our outstanding shares of common stock.

EXPERTS

The financial statements and schedule as of December 31, 2015 and 2014 and for each of the three years in the period ended December 31, 2015 and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2015 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 (the report on the effectiveness of internal control over financial reporting expresses an adverse opinion on the effectiveness of the company's internal control over financial reporting as of December 31, 2015), incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

Table of Contents

	Shares of Common Stock	
Warrants to Purchase		Shares of Common Stock

PROSPECTUS SUPPLEMENT

Rodman & Renshaw
a unit of H.C. Wainwright & Co.

July , 2016