

CYTRX CORP
Form 424B2
October 10, 2013
Table of Contents

Filed Pursuant to Rule 424(b)(2)

Registration No. 333-185308

PROSPECTUS SUPPLEMENT
(To the Prospectus dated December 21, 2012)

10,000,000 Shares

Common Stock

We are offering 10,000,000 shares of our common stock, par value \$0.001 per share, pursuant to this prospectus supplement and the accompanying prospectus.

Our common stock is listed on The NASDAQ Capital Market under the symbol CYTR. On October 8, 2013, the closing price of our common stock was \$2.74 per share.

Our business and an investment in our common stock involve significant risks. See Risk Factors beginning on page S-8 of this prospectus supplement and on page 7 of the accompanying prospectus.

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

	Per Share	Total
Public offering price	\$ 2.25	\$ 22,500,000
Underwriting discount	\$ 0.135	\$ 1,350,000
Proceeds, before expenses, to us	\$ 2.115	\$ 21,150,000

We have granted a 30-day option to the underwriters solely to cover over-allotments, if any.

Edgar Filing: CYTRX CORP - Form 424B2

The underwriters expect to deliver the shares against payment therefor on or about October 15, 2013.

Sole Book-Running Manager

Aegis Capital Corp

Co-Lead Manager

H.C. Wainwright & Co., LLC

October 8, 2013

Table of Contents

TABLE OF CONTENTS
PROSPECTUS SUPPLEMENT

<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</u>	S-3
<u>RISK FACTORS</u>	S-8
<u>USE OF PROCEEDS</u>	S-18
<u>DIVIDEND POLICY</u>	S-18
<u>CAPITALIZATION</u>	S-19
<u>DILUTION</u>	S-20
<u>UNDERWRITING</u>	S-22
<u>LEGAL MATTERS</u>	S-29
<u>EXPERTS</u>	S-29
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	S-29
<u>INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE</u>	S-29
PROSPECTUS	

<u>ABOUT THIS PROSPECTUS</u>	1
<u>NOTE ON FORWARD-LOOKING STATEMENTS</u>	2
<u>ABOUT CYTRX</u>	3
<u>RISK FACTORS</u>	7
<u>DIVIDEND POLICY</u>	18
<u>THE SECURITIES THAT WE MAY OFFER</u>	18
<u>DESCRIPTION OF CAPITAL STOCK</u>	18
<u>DESCRIPTION OF WARRANTS</u>	21
<u>DESCRIPTION OF UNITS</u>	23
<u>PLAN OF DISTRIBUTION</u>	23
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	25

<u>INCORPORATION OF INFORMATION FILED WITH THE SEC</u>	25
<u>LEGAL MATTERS</u>	26
<u>EXPERTS</u>	26

Table of Contents

ABOUT THIS PROSPECTUS SUPPLEMENT

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

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

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

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

In this prospectus supplement and in the accompanying prospectus, we sometimes refer to CytRx Corporation as CytRx, to our former subsidiary, RXi Pharmaceuticals Corporation, as RXi, and to our former subsidiary, Innovive Pharmaceuticals, Inc., which we acquired in September 2008 and merged into CytRx in December 2008, as Innovive. References in this prospectus supplement and in the accompanying prospectus to we, us, our or the company refer to CytRx, alone, unless otherwise indicated.

NOTE ON FORWARD-LOOKING STATEMENTS

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

S-1

Table of Contents

limited to, those factors set forth under the caption "Risk Factors" in this prospectus supplement and in the accompanying prospectus and under the captions "Risk Factors," "Business," "Legal Proceedings," "Management's Discussion and Analysis of Financial Condition and Results of Operations," "Quantitative and Qualitative Disclosures About Market Risk" and "Controls and Procedures" in our most recent Annual Report on Form 10-K and Quarterly Report on Form 10-Q, all of which you should review carefully. Please consider our forward-looking statements in light of those risks as you read this prospectus supplement and the accompanying prospectus. We undertake no obligation to publicly update or review any forward-looking statement, whether as a result of new information, future developments or otherwise.

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

INDUSTRY DATA

Unless otherwise indicated, information contained or incorporated by reference in this prospectus supplement or the accompanying prospectus concerning our industry, including our general expectations and market opportunity, is based on information from our own management estimates and research, as well as from industry and general publications and research, surveys and studies conducted by third parties. Management estimates are derived from publicly available information, our knowledge of our industry and assumptions based on such information and knowledge, which we believe to be reasonable. In addition, assumptions and estimates of our and our industry's future performance are necessarily subject to a high degree of uncertainty and risk due to a variety of factors, including those described in "Risk Factors" beginning on page S-8 of this prospectus supplement and on page 7 of the accompanying prospectus. These and other factors could cause our future performance to differ materially from our assumptions and estimates.

TRADEMARKS

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

Table of Contents**SUMMARY**

This summary highlights selected information about us, this offering and information contained or incorporated by reference in this prospectus supplement or in the accompanying prospectus. This summary is not complete and does not contain all of the information that may be important to you and that you should consider before purchasing our shares. This prospectus supplement and the accompanying prospectus include or incorporate by reference information about our shares, as well as information regarding our business and detailed financial data. Before making an investment decision, to fully understand this offering and its consequences to you, you should carefully read this entire prospectus supplement and the accompanying prospectus, including Risk Factors beginning on page S-8 of this prospectus supplement and page 7 of the accompanying prospectus, and the financial statements, related notes and other information that we incorporated by reference herein, including our Annual Report on Form 10-K for the fiscal year ended December 31, 2012 and our Quarterly Report on Form 10-Q for the quarter ended June 30, 2013.

The Company**Overview**

We are a biopharmaceutical research and development company specializing in oncology. We currently are focused on the clinical development of aldoxorubicin (formerly known as INNO-206), our modified version of the widely-used chemotherapeutic agent, doxorubicin. We are conducting a global Phase 2b clinical trial with aldoxorubicin as a treatment for soft tissue sarcoma, have completed a Phase 1b/2 clinical trial primarily in the same indication, a Phase 1b study of aldoxorubicin in combination with doxorubicin in patients with advanced solid tumors, and a Phase 1b pharmacokinetics clinical trial in patients with metastatic solid tumors. We plan to initiate under a Special Protocol Assessment, or SPA, granted by the U.S. Food and Drug Administration, or FDA, a potential pivotal Phase 3 global trial of aldoxorubicin as a therapy for patients with soft tissue sarcoma whose tumors have progressed following treatment with chemotherapy. We also are initiating Phase 2 clinical trials with aldoxorubicin in patients with late-stage glioblastoma (brain cancer) and AIDS-related Kaposi's sarcoma. We plan to expand our pipeline of oncology candidates based on a linker platform technology that can be utilized with multiple chemotherapeutic agents and may allow for greater concentration of drug at tumor sites. We also have rights to two additional drug candidates, tamibarotene and bafetinib. We completed our evaluation of bafetinib in the ENABLE Phase 2 clinical trial in high-risk B-cell chronic lymphocytic leukemia (B-CLL), plan to seek a partner for further development of bafetinib.

Our Product Candidate Pipeline

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

	Product	Indication(s)	Stage of development
Technology	candidate		
Doxorubicin conjugate	Aldoxorubicin	Soft tissue sarcoma	Phase 3 1Q14 Phase 2b ongoing
		Glioblastoma multiforme	Phase 2 4Q13
		Kaposi's sarcoma	Phase 2 4Q13 Phase 1b complete

In combination with
doxorubicin in patients
with advanced solid
tumors

Our Clinical Development Programs

Our current clinical development programs are summarized below.

Aldoxorubicin

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

S-3

Table of Contents

Aldoxorubicin for the Treatment of Cancer. Anthracyclines are a class of drugs that are among the most commonly used agents in the treatment of cancer. Doxorubicin, the first anthracycline to gain FDA approval, has demonstrated efficacy in a wide variety of cancers, including breast cancer, lung cancer, sarcomas, and lymphomas. However, due to the uptake of doxorubicin by various parts of the body, it is associated with side effects such as cumulative cardiotoxicity, myelosuppression (decreased production of blood cells by bone marrow), gastrointestinal disorders, mucositis (inflammation of the mucous membranes lining the mouth and digestive tract), stomatitis (inflammation of soft tissue of the mouth), and extravasation (the leakage of intravenous drugs from the vein into the surrounding tissue).

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

Our postulated mechanism of action for aldoxorubicin is as follows:

after administration, aldoxorubicin rapidly binds circulating albumin through the EMCH linker;

circulating albumin preferentially accumulates in tumors, bypassing concentration in other non-tumor sites, including the heart, liver and gastrointestinal tract due to a mechanism called Enhanced Permeability and Retention by Solid Tumors ;

once albumin-bound aldoxorubicin reaches the tumor, the acidic environment of the tumor causes cleavage of the acid-sensitive linker; and

free doxorubicin is released at the site of the tumor and is taken up by the cancer cells.

Pre-clinical data. In a variety of preclinical models, aldoxorubicin was superior to doxorubicin at equitoxic doses in its ability to allow an increase in the total doxorubicin dose, its antitumor efficacy and its safety. Toxicology studies in rodents also demonstrated a reduction in cardiotoxicity. Animal studies conducted by aldoxorubicin inventor Dr. Felix Kratz of the Department of Medical Oncology, Clinical Research, at the Tumor Biology Center in Freiburg, Germany, demonstrated statistically significant efficacy compared to either placebo or native doxorubicin against breast, ovarian, pancreatic and small cell lung cancers growing in immunodeficient mice.

We also recently announced additional data from a study of aldoxorubicin in immunodeficient mice transplanted with human glioblastoma cells in their brain that showed those animals treated with aldoxorubicin had a median survival rate of more than 63 days, compared with approximately 25 days for animals treated with doxorubicin or saline. The data also indicated evidence of drug concentration inside tumors growing in the brain and significant tumor regression in aldoxorubicin-treated animals, while doxorubicin did not appear to enter the tumor to any significant degree and showed little or no efficacy in the treatment of these brain tumors. Aldoxorubicin significantly reduced the number of dividing cells within the brain tumors in this trial and showed a statistically relevant increased expression of apoptosis or cell death markers.

Clinical data. A Phase 1 study of aldoxorubicin that demonstrated safety and objective clinical responses in several tumor types was completed in 2005 and presented at the March 2006 Krebskongress meeting in Berlin. In this study,

doses were administered every three weeks at up to six times the standard dose of doxorubicin without an increase in the types of side effects compared with those historically observed with native doxorubicin. Twenty-three of thirty-five evaluable patients had either an objective clinical (partial) response or stable disease. Objective clinical responses were observed in patients with sarcoma, breast and small cell lung cancers.

We completed a Phase 1b/2 clinical trial with aldoxorubicin in patients with advanced solid tumors and presented favorable data at the American Society for Clinical Oncology Meeting in June 2012. In that Phase 1b/2 clinical trial, clinical benefit (defined as partial response or stable disease of more than four months following up to eight cycles of treatment) with aldoxorubicin at the maximum tolerated dose was shown in ten of 13 (76.9%) evaluable patients with relapsed or refractory soft tissue sarcoma.

In addition, best responses for the 13 evaluable soft tissue sarcoma trial subjects included the following: five (38.5%) achieved partial response, as defined as shrinkage of target tumors of more than 30%; seven (53.8%) showed prolonged stable disease (defined as tumor shrinkage <30% from baseline or tumor growth <20% from the nadir); eight (61.5%) had tumor shrinkage; and five of eight patients (62.5%) who demonstrated either partial responses or prolonged stable disease after treatment with aldoxorubicin had

Table of Contents

been previously treated with doxorubicin and had failed to respond. There were no observed cardiac toxicities and no drug-related patient deaths. The most common adverse event, neutropenia, also observed with doxorubicin treatment, resolved prior to the start of the next treatment. Median estimated progression-free survival for advanced soft tissue sarcoma patients in the trial was 6.4 months with a range of 1.0 to more than 10.7 months.

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

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

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

The Phase 2b clinical trial with aldoxorubicin in patients with soft tissue sarcoma is an international trial under the direction of Sant P. Chawla, M.D., F.R.A.C.P., Director of the Sarcoma Oncology Center in Santa Monica, California. The Phase 2b clinical trial's primary objectives are to measure the progression-free survival, tumor response and overall survival of patients with advanced soft tissue sarcomas treated with aldoxorubicin. This clinical trial also will assess the safety of aldoxorubicin compared to doxorubicin in this patient population through a number of indicators, including the frequency and severity of adverse events.

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

We plan to initiate in 2013 a Phase 2 clinical trial to evaluate the preliminary efficacy and safety of aldoxorubicin in patients with unresectable glioblastoma whose tumors have progressed following prior treatment with surgery, radiation and with the drug temozolomide. The clinical trial is expected to enroll approximately 28 patients at sites including the John Wayne Cancer Center in Santa Monica, California, City of Hope in Duarte, California, and the LSU Medical Center in New Orleans, Louisiana.

We also plan to initiate in 2013 a Phase 2 clinical trial evaluating the preliminary efficacy of aldoxorubicin in patients with AIDS-related Kaposi's sarcoma, a common HIV-associated tumor. The current standard-of-care for severe dermatological and systemic Kaposi's sarcoma is liposomal doxorubicin (Doxil®); however, a significant proportion of patients exhibit minimal or no clinical response to this agent, and the drug's toxicity often prevents continued therapy. The Phase 2 trial will enroll up to 30 patients and will be conducted at the LSU Medical Center in New Orleans, Louisiana.

In 2012, we completed a Phase 2 trial for patients with advanced pancreatic ductal adenocarcinomas who had relapsed or failed to respond to two prior regimens, one regimen containing gemcitabine (Gemzar®) and the other a fluoropyrimidine such as 5-fluorouracil. No objective clinical responses were observed in 14 patients treated with native idoxorubicin, and we are considering testing the idoxorubicin in combination with the commonly-prescribed drug Abraxane as a second-line treatment in that indication.

Bafetinib

Bafetinib (formerly INNO-406) is an orally bioavailable, rationally-designed inhibitor of several Src kinases developed by the Japanese pharmaceutical company Nippon Shinyaku, to overcome some of the limitations of Gleevec and other tyrosine kinase inhibitors in resistant chronic myelogenous leukemia, or CML. In addition to its Bcr-Abl inhibitory properties, bafetinib is a potent and specific inhibitor of Lyn and Fyn kinases. These kinases are reported to be involved in both solid and hematological cancers. Lyn kinase's involvement in the B-cell signaling pathway led us to evaluate bafetinib in B-cell malignancies such as chronic lymphocytic leukemia, or CLL. We hold rights to bafetinib in all territories, except in Japan.

Table of Contents

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

Tamibarotene

Tamibarotene is an orally available, synthetic retinoid rationally designed to overcome resistance and reduce the toxic side effects of differentiation therapy with all-trans retinoic acid, or ATRA, a component of the current first-line treatment for acute promyelocytic leukemia, or APL. We ceased our Phase 2b clinical trial of tamibarotene in patients with non-small-cell lung cancer after it failed to show efficacy.

Reverse Stock Split

On May 16, 2012, we effected a 1-for-7 reverse stock split of our outstanding shares of common stock and our common stock began trading on The NASDAQ Capital Market on a split-adjusted basis. All share and per share amounts in this prospectus supplement have been adjusted to reflect the reverse stock split as if it had occurred at the beginning of the earliest period presented.

Corporate Information

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

Table of Contents

The Offering

Securities offered by us	10,000,000 shares of common stock
Common stock to be outstanding after this offering	40,608,392 shares of common stock
Use of proceeds	We intend to use the net proceeds of this offering to fund our clinical trials of aldoxorubicin and for general corporate purposes, which may include working capital, capital expenditures and research and development and other commercial expenditures. See Use of Proceeds on page S-18 for further information.
Risk factors	See Risk Factors beginning on page S-8 of this prospectus supplement and page 7 of the accompanying prospectus for a discussion of factors you should read and consider carefully before investing in our common stock.
NASDAQ Capital Market symbol	CYTR

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

based on 30,608,392 shares outstanding on September 30, 2013;

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

excludes 3,406,881 shares of our common stock subject to options outstanding as of September 30, 2013 having a weighted-average exercise price of \$4.15 per share;

excludes 2,595,701 shares of our common stock that have been reserved for issuance in connection with future grants under our stock option plans as of September 30, 2013; and

excludes 8,083,181 shares of our common stock that have been reserved for issuance upon exercise of outstanding warrants as of September 30, 2013 having a weighted-average exercise price of \$4.91 per share.

S-7

Table of Contents

RISK FACTORS

You should carefully consider the risks described below before making an investment decision. The risks described below are not the only ones we face. Additional risks we are not presently aware of or that we currently believe are immaterial may also impair our business operations. Our business could be harmed by any of these risks. The trading price of our common stock could decline due to any of these risks, and you may lose all or part of your investment. In assessing these risks, you should also refer to the other information contained or incorporated by reference into this prospectus supplement and the accompanying prospectus, including our financial statements and related notes. We have attempted to identify below the major factors that could cause differences between actual and planned or expected results, but we cannot assure you that we have identified all such factors. Please also see page 7 of the accompanying prospectus for additional risk factors.

Risks Associated With Our Business

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

We have operated at a loss due to our ongoing expenditures for research and development of our product candidates and for general and administrative purposes and lack of significant recurring revenue. We incurred a net loss of approximately \$18.0 million for the year ended December 31, 2012 and of approximately \$10.3 million for the six months ended June 30, 2013, and had an accumulated deficit as of June 30, 2013 of approximately \$239.2 million. We will continue to incur losses unless and until we are able to commercialize aldoxorubicin or one or more of our other current or future product candidates. These losses, among other things, have had and will continue to have an adverse effect on our stockholders' equity and working capital. Because of the numerous risks and uncertainties associated with our product development efforts, we are unable to predict when we may become profitable, if at all. If we do not become profitable or are unable to maintain future profitability, the market value of our common stock will be adversely affected.

Because we have no source of significant recurring revenue, we must depend on financing to sustain our operations.

Developing products and conducting clinical trials require substantial amounts of capital. To date, we have relied primarily upon proceeds from sales of our equity securities, sales of our shares of common stock of our former RXi subsidiary and the exercise of options and warrants to generate funds needed to finance our business and operations. We will need to raise additional capital to, among other things:

fund our clinical trials and pursue regulatory approval of aldoxorubicin and our other existing and possible future product candidates;

expand our research and development activities;

finance our general and administrative expenses;

acquire or license new technologies;

prepare, file, prosecute, maintain, enforce and defend our patent and other proprietary rights; and

develop and implement sales, marketing and distribution capabilities to successfully commercialize any product for which we obtain marketing approval and choose to market ourselves.

Our revenue was \$100,000 for the year ended December 31, 2012 and \$200,000 for the six months ended June 30, 2013. We will have no significant recurring revenue unless we are able to commercialize aldorubicin, our lead product candidate, or one of our preclinical candidates, either of which may require us to first enter into strategic arrangements with third parties.

At June 30, 2013, we had cash and cash equivalents of approximately \$11.0 million and short-term investments of \$17.0 million. Management believes that our current resources, together with the net proceeds from this offering, will be sufficient to fund our operations for the foreseeable future. These expectations are based upon numerous assumptions and subject to many uncertainties, and our actual experience may be significantly different from these expectations.

If we obtain marketing approval and successfully commercialize aldorubicin or other product candidate, we anticipate it will take a minimum of several years, and likely longer, for us to generate significant recurring revenue, and we will be dependent on future financing until such time, if ever, as we can generate significant recurring revenue. Our ability to raise capital may be adversely

Table of Contents

affected by the weak economic recovery in the United States. We have no commitments from third parties to provide us with any additional financing, and we may not be able to obtain future financing on favorable terms, or at all. Failure to obtain adequate financing would adversely affect our ability to operate as a going concern. If we raise additional funds by issuing equity securities, dilution to stockholders may result and new investors could have rights superior to holders of the shares issued in this offering. In addition, debt financing, if available, may include restrictive covenants. If adequate funds are not available to us, we may have to liquidate some or all of our assets or to delay or reduce the scope of or eliminate some portion or all of our development programs or clinical trials. We also may have to license to other companies our product candidates or technologies that we would prefer to develop and commercialize ourselves.

If we do not achieve our projected development goals in the time frames we estimate, the commercialization of our products may be delayed and our business prospects may suffer. Our financial projections also may prove to be materially inaccurate.

From time to time, we estimate the timing of the accomplishment of various scientific, clinical, regulatory and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of scientific studies and clinical trials and the submission of regulatory filings such as the discussion in this prospectus supplement of the expected timing of certain milestones relating to our aldoxorubicin clinical development programs.

We also may disclose projected expenditures or other forecasts for future periods. These and other financial projections are based on management's current expectations and do not contain any margin of error or cushion for any specific uncertainties, or for the uncertainties inherent in all financial forecasting.

The actual timing of milestones and actual expenditures or other financial results can vary dramatically compared to our estimates, in some cases for reasons beyond our control. If we do not meet milestones or financial projections as announced from time to time, the development and commercialization of our products may be delayed and our business prospects may suffer. The assumptions management has used to produce these projections may significantly change or prove to be inaccurate. Accordingly, you should not unduly rely on any of these financial projections.

If our products are not successfully developed and approved by the FDA or foreign regulatory authorities, we may be forced to reduce or curtail our operations.

All of our product candidates in development must be approved by the FDA or corresponding foreign governmental agencies before they can be marketed. The process for obtaining FDA and foreign government approvals is both time-consuming and costly, with no certainty of a successful outcome. This process typically includes the conduct of extensive pre-clinical and clinical testing, including post-approval testing, which may take longer or cost more than we or our licensees, if any, anticipate, and may prove unsuccessful due to numerous factors. Product candidates that may appear to be promising at early stages of development may not successfully reach the market for a number of reasons. The results of preclinical and initial clinical testing of these product candidates may not necessarily be predictive of the results that will be obtained from later or more extensive testing. Companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in advanced clinical trials, even after obtaining promising results in earlier trials.

Numerous factors could affect the timing, cost or outcome of our product development efforts, including the following:

difficulty in enrolling patients in conformity with required protocols or projected timelines;

requirements for clinical trial design imposed by the FDA;

unexpected adverse reactions by patients in trials;

difficulty in obtaining clinical supplies of the product;

changes in or our inability to comply with FDA or foreign governmental product testing, manufacturing or marketing requirements;

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

S-9

Table of Contents

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.

In addition, on October 1, 2013, the U.S. federal government suspended services deemed non-essential as a result of the failure by Congress to enact regular appropriations for the 2014 fiscal year. If the shutdown continues for a prolonged period of time, it could result in significant delays in the FDA's ability to timely review and process any submissions we have filed or may file, or cause other regulatory delays, which could have a material adverse effect on our business.

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

Furthermore, even if we obtain regulatory approvals, our products and the manufacturing facilities used to produce them will be subject to continual review, including periodic inspections and mandatory post-approval clinical trials by the FDA and other U.S. and foreign regulatory authorities. Any delay or failure in obtaining required approvals or to comply with post-approval regulatory requirements could have a material adverse effect on our ability to generate revenue from the particular product candidate. The failure to comply with any post-approval regulatory requirements also could result in the rescission of the related regulatory approvals or the suspension of sales of the offending product.

Our current and planned clinical trials of our lead product candidate may fail to show that it is clinically safe and effective, or that it is better than alternative treatments.

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

Top-line data from our Phase 2b clinical trial of aldoxorubicin as a treatment for soft tissue sarcomas may differ from our recently announced preliminary data. Even if our current trials are successful, subsequent trials may not yield statistically significant data indicating that aldoxorubicin is clinically effective. Accordingly, we, or any development partners, may ultimately be unable to provide the FDA with satisfactory data on clinical safety and efficacy sufficient to obtain FDA approval of aldoxorubicin for any indication.

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

We have an SPA with the FDA for the pivotal trial of aldoxorubicin for the treatment of soft-tissue sarcomas. The SPA means that the FDA agrees with the design, execution, and analyses proposed in a protocol, and constitutes a commitment that the FDA will not subsequently change its perspectives on these matters, unless a previously

unrecognized public or animal health concern were to arise or changes were to be made to the protocol, itself. Even under a SPA, marketing approval by the FDA is not guaranteed, because a final determination that the agreed-upon protocol satisfies a specific objective, such as the demonstration of efficacy and safety (positive benefit-risk ratio), or supports an approval decision, will be based on a complete review of all the data submitted to the FDA.

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

We do not have the facilities or expertise to manufacture supplies of aldoxorubicin or any of our other product candidates. Accordingly, we are dependent upon third-party manufacturers, or potential future strategic alliance partners, to manufacture these supplies. We have manufacturing supply arrangements in place with respect to a portion of the clinical supplies needed for the clinical development programs for aldoxorubicin. However, we have no supply arrangements for the commercial manufacture of this product candidate or any manufacturing supply arrangements for any other potential product candidates, and we may not be able to secure needed supply arrangements on attractive terms, or at all. Our failure to secure these arrangements as needed could have a materially adverse effect on our ability to complete the development of our products or to commercialize them.

If aldoxorubicin, our lead product candidate, or our other product candidates cannot be manufactured in suitable quantities and in accordance with regulatory standards, our clinical trials, regulatory approvals and marketing efforts for such products may be delayed. Such delays could adversely affect our competitive position and our chances of generating significant recurring revenues. If any of our products that are approved for marketing cannot be manufactured at an acceptable cost, the commercial success of such product candidates may be adversely affected.

Table of Contents

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

The completion of the development of aldoxorubicin or our other product candidates, as well as marketing and commercialization, may require us to enter into strategic alliances or other collaborative arrangements with other pharmaceutical companies under which those companies will be responsible for one or more aspects of the eventual marketing and commercialization of our products.

Our products, if approved for marketing, may not have sufficient potential commercial value to enable us to secure strategic arrangements with suitable companies on attractive terms, or at all. If we are unable to enter into such arrangements, we may not have the financial or other resources to complete the development of any of our products and may have to sell our rights in them to a third party or abandon their development altogether.

To the extent we enter into collaborative arrangements, we will be dependent upon the timeliness and effectiveness of the development and marketing efforts of our contractual partners. If these companies do not allocate sufficient personnel and resources to these efforts or encounter difficulties in complying with applicable FDA and other regulatory requirements, we may not obtain regulatory approvals as planned, if at all, and the timing of receipt or the amount of revenue from these arrangements may be materially and adversely affected. By entering into these arrangements rather than completing the development and then marketing these products on our own, the profitability to us of these products may decline.

We may be unable to protect our intellectual property rights, which could adversely affect our ability to compete effectively.

We will be able to protect our technologies from unauthorized use by third parties only to the extent that we have rights to valid and enforceable patents or other proprietary rights that cover them. Although we have rights to patents and patent applications directed to aldoxorubicin and other product candidates, these patents and applications may not prevent third parties from developing or commercializing similar or identical technologies. In addition, our patents may be held to be invalid if challenged by third parties, and our patent applications may not result in the issuance of patents.

The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in biotechnology patents has emerged to date in the United States and in many foreign countries. The application and enforcement of patent laws and regulations in foreign countries is even more uncertain. Accordingly, we may not be able to effectively file, protect or defend our proprietary rights on a consistent basis. Many of the patents and patent applications on which we rely were issued or filed by third parties prior to the time we acquired rights to them. The validity, enforceability and ownership of those patents and patent applications may be challenged, and if a court decides that our patents are not valid, we will not have the right to stop others from using our inventions. There is also the risk that, even if the validity of our patents is upheld, a court may refuse to stop others on the ground that their activities do not infringe our patents.

Any litigation brought by us to protect our intellectual property rights could be costly and have a material adverse effect on our operating results or financial condition, make it more difficult for us to enter into strategic alliances with third parties to develop our products, or discourage our existing licensees from continuing their development work on our potential products. If our patent coverage is insufficient to prevent third parties from developing or commercializing similar or identical technologies, the value of our assets is likely to be materially and adversely affected.

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

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

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

Table of Contents

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

we may become involved in time-consuming and expensive litigation, even if the claim is without merit;

we may become liable for substantial damages for past infringement if a court decides that our technology infringes a competitor's patent;

a court may prohibit us from selling or licensing our product without a license from the patent holder, which may not be available on commercially acceptable terms, if at all, or which may require us to pay substantial royalties or grant cross licenses to our patents; and

we may have to redesign our product candidates or technology so that it does not infringe patent rights of others, which may not be possible or commercially feasible.

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

Any products we develop may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, which could have a material adverse effect on our business.

We intend to sell our products that may be approved for marketing primarily to hospitals, which receive reimbursement for the health care services they provide to their patients from third-party payors, such as Medicare, Medicaid and other domestic and international government programs, private insurance plans and managed care programs. Most third-party payors may deny reimbursement if they determine that a medical product was not used in accordance with cost-effective treatment methods, as determined by the third-party payor, or was used for an unapproved indication. Third-party payors also may refuse to reimburse for experimental procedures and devices. Furthermore, because our programs are in the early stages of development, we are unable at this time to determine their cost-effectiveness and the level or method of reimbursement. Increasingly, the third-party payors who reimburse patients are requiring that drug companies provide them with predetermined discounts from list prices, and are challenging the prices charged for medical products. If the price we are able to charge for any products we develop is inadequate in light of our development and other costs, our profitability could be adversely affected.

We currently expect that any drugs we develop may need to be administered under the supervision of a physician. Under currently applicable law, drugs that are not usually self-administered may be eligible for coverage by the Medicare program if:

they are incidental to a physician's services;

they are reasonable and necessary for the diagnosis or treatment of the illness or injury for which they are administered according to accepted standard of medical practice;

they are not excluded as immunizations; and

they have been approved by the FDA.

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

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

S-12

Table of Contents

Patients with glioblastoma multiforme (GBM) generally undergo invasive brain surgery, although disease progression following surgery is nearly 100%. The front-line therapy for GBM following surgery is Temozolomide (Temodar®) in combination with radiation. Bevacizumab (Avastin®) has been approved for the treatment of GBM in patients failing Temodar®. Drugs in development to treat GBM include rindopepimut by Celldex Therapeutics, DCVax by Northwest Biotherapeutics, TRC105 from Tracoon Pharmaceuticals, and buparlisib by Novartis. Kaposi's sarcoma is generally treated with radiation, surgery and/or liposomal doxorubicin. Other drugs in development for Kaposi's sarcoma include selumetinib by AstraZeneca and pomalidamide by Celgene.

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

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

commercially reasonable royalties based on a percentage of net sales (as defined in the agreement);

a percentage of non-royalty sub-licensing income (as defined in the agreement); and

milestones of \$1,000,000 for each additional final marketing approval that we might obtain.

Table of Contents

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

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

commercially reasonable royalties based on a percentage of net sales (as defined in the agreement), dependent on reaching certain revenue thresholds;

annual minimum payments if sales of bafetinib do not meet specified levels; and

a percentage of non-royalty sub-licensing income (as defined in the agreement).

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

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

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

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

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

We may seek to acquire additional technologies by licensing or purchasing such technologies, or through a merger or acquisition of one or more companies that own such technologies. We have no current understanding or agreement to

acquire any technologies, however, and we may not be able to identify or successfully acquire any additional technologies. We also may seek to acquire products from third parties that already are being marketed or have been approved for marketing, although we have not currently identified any of these products. We do not have any prior experience in acquiring or marketing products approved for marketing and may need to find third parties to market any products that we might acquire.

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

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

Table of Contents

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