

CYTRX CORP
Form 424B5
July 28, 2009

Filed Pursuant to Rule 424(b)(5)
Registration Statement No. 333-147605
PROSPECTUS SUPPLEMENT NO. 1
(To Prospectus dated July 23, 2009)

CYTRX CORPORATION

Up to 15,252,040 Shares of Common Stock, par value \$0.001 per share

Warrants to Purchase up to 3,813,010 Shares of Common Stock, par value \$0.001 per share

This prospectus supplement and the accompanying prospectus relate to the sale of up to 15,252,040 shares of our common stock and warrants to purchase up to 3,813,010 shares of our common stock and the issuance of up to 3,813,010 shares of our common stock upon exercise of the warrants. Purchasers will receive warrants to purchase 0.25 share of common stock at an exercise price of \$1.70 per share for each share of common stock they purchase in this offering. The shares of common stock and the warrants will be issued separately. One Series A Junior Participating Preferred Stock Purchase Right that trades with our common stock will accompany each share of our common stock being offered.

Our common stock is listed on the Nasdaq Capital Market under the symbol "CYTR." On July 24, 2009, the last reported sale price of our common stock on the Nasdaq Capital Market was \$1.21 per share.

Rodman & Renshaw, LLC acted as the placement agent in connection with this offering. The placement agent is not purchasing or selling any of the securities offered nor is it required to sell any specific number or dollar amount of securities, but has agreed to use its reasonable best efforts to sell all of the securities offered by this prospectus supplement. We have agreed to pay the placement agent the placement agent fees set forth in the table below and to issue to the placement agent warrants to purchase up to 915,122 shares of our common stock at an exercise price of \$1.70 per share. The placement agent warrants and underlying warrant shares are not covered by this prospectus supplement.

	Per Unit	Aggregate Offering
Public offering price	\$1.31	\$20,000,000
Placement agent fees	\$0.08	\$1,200,000
Proceeds, before expenses, to us	\$1.23	\$18,800,000

We expect delivery of the shares of common stock and the warrants being sold in this offering to be made to the purchasers no later than July 31, 2009, against payment of immediately available funds.

An investment in our securities involves a high degree of risk. Before purchasing any securities, you should consider carefully the risks referred to in the "Risk Factors" section beginning on page S-4 of 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.

Rodman & Renshaw

The date of this prospectus supplement is July 28, 2009

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement supplements the accompanying prospectus, which is part of our Registration Statement on Form S-3, as amended, (registration statement no. 333-147605), filed with the Securities and Exchange Commission, or SEC, utilizing the “shelf” registration process. Under the shelf registration process, we may offer to sell securities from time to time in one or more transactions. This prospectus supplement describes the specific terms of this offering. The accompanying prospectus, including the information incorporated by reference, provides general information about us and about the shares we may offer in the shelf registration process.

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

In this prospectus supplement and the accompanying prospectus, we sometimes refer to CytRx Corporation as “CytRx” and to our former subsidiary, RXi Pharmaceuticals Corporation, as “RXi.” References in this prospectus supplement and in the accompanying prospectus to the “company,” “we,” “us” or “our” refer to CytRx, alone.

SUMMARY

This summary highlights selected information about this offering. This summary is not complete and does not contain all the information you should consider before purchasing our securities in this offering. Before purchasing any of our securities, you should read carefully this entire prospectus supplement and the accompanying prospectus, including the information in the “Risk Factors” sections in this prospectus supplement and in the accompanying prospectus and the financial statements and other information that we incorporate by reference in the accompanying prospectus.

About CytRx Corporation

We are a biopharmaceutical research and development company engaged in the development of high-value human therapeutics. Our drug development pipeline includes three product candidates in clinical development for cancer indications, including registration studies of tamibarotene for the treatment of acute promyelocytic leukemia, or APL. In addition to our core oncology programs, we are developing treatments for neurodegenerative and other disorders based upon our small-molecule molecular chaperone amplification technology. Apart from our drug development programs, we maintain at present a 45% equity interest in our former subsidiary, RXi Pharmaceuticals Corporation, or RXi (NASDAQ: RXII).

On September 19, 2008, we completed the merger acquisition of Innovive Pharmaceuticals, Inc., or Innovive, and its clinical-stage oncology product candidates, including tamibarotene. As a result of the merger, Innovive became our wholly owned subsidiary. On December 30, 2008, we merged the former Innovive subsidiary into CytRx. Prior to our acquisition of Innovive, we were focused on developing human therapeutics based primarily upon our small-molecule molecular chaperone amplification technology, including arimoclomol for amyotrophic lateral sclerosis, which is commonly known as ALS or Lou Gehrig’s disease, and iroxanadine for diabetic foot ulcers and other potential indications. After acquiring Innovive, we redirected our efforts to developing Innovive’s lead oncology product candidates, tamibarotene for APL, INNO-206 for small cell lung cancer, or SCLC, and other solid tumor cancers, and bafetinib, which we believe hold greater near-term revenue potential than our molecular chaperone product candidates. Our current business strategy is to seek one or more strategic partnerships for the further development of arimoclomol and iroxanadine.

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.

The Offering

Common stock offered by us	15,252,040 shares.
Common shares to be outstanding immediately after this offering	108,605,005 shares.
Warrants offered by us	Warrants to purchase up to 3,813,010 shares of our common stock, which excludes the warrants to purchase up to an aggregate of 915,122 shares of our common stock issuable to the placement agent in this offering that are not covered by this prospectus supplement. The warrants will have an exercise price of \$1.70 per share and will be exercisable at any time after the date of their issuance and on or before the fifth anniversary of their initial exercise date. This prospectus supplement also relates to the offering of the shares of common stock issuable upon exercise of the warrants.
Use of proceeds	We intend to use the net proceeds of this offering for research and development, including clinical development of our lead product candidate, tamiboratene, for the treatment of APL, and clinical and preclinical research and development with respect to other potential product candidates. We also intend to use the net proceeds for working capital and general corporate purposes, which may include our acquisition, in-licensing or investment in complementary products, product candidates, technologies or companies. See the “Use of Proceeds” section of this prospectus supplement for more information about the estimated net proceeds of this offering.
Nasdaq Capital Market symbol	CYTR.
Risk factors	An investment in our securities involves a high degree of risk. See the “Risk Factors” sections in this prospectus supplement and in the accompanying prospectus for more information regarding some of these risks and uncertainties.

The total shares of common stock outstanding immediately before and after this offering is based on 93,352,965 shares outstanding as of July 24, 2009, and excludes:

- 11,434,848 shares of our common stock issuable upon exercise of outstanding warrants as of that date at a weighted-average exercise price of \$1.32 per share;
- 7,061,847 shares of our common stock issuable upon exercise of outstanding stock options as of that date at a weighted-average exercise price of \$1.12 per share;
- 10,940,532 shares of our common stock available for issuance with respect to future grants under our stock incentive plans;
- 3,813,010 shares of our common stock issuable upon the exercise of warrants to be issued to purchasers in this offering at an exercise price of \$1.70 per share; and

- 915,122 shares of common stock issuable upon exercise of the placement agent warrants to be issued in connection with this offering at an exercise price of \$1.70 per share, which shares are not covered by this prospectus supplement.

RISK FACTORS

An investment in our securities involves a high degree of risk. Prior to making a decision about purchasing our securities, you should carefully consider the risks and uncertainties and all other information contained or incorporated by reference in this prospectus supplement and in the accompanying prospectus. These include the “Risks Associated With Our Business,” “Risks Associated With Our Investment in RXi,” and “Risks Associated With Our Common Stock” discussed in the “Risk Factors” section in the accompanying prospectus and the “Risks Associated With This Offering” discussed below in this section, as well as any modification, replacement or update to these risks and uncertainties that are reflected in any subsequent filings we make with the SEC as described in the “Where You Can Find More Information” section of this prospectus supplement. These risks and uncertainties are not the only ones facing us. Additional risks and uncertainties not presently known to us, or that we currently perceive as immaterial, may also harm our business. If any of these risks or uncertainties actually occurs, our business, results of operations and financial condition could be materially and adversely affected. In that case, the trading price of our common stock could decline, and you could lose all or part of your investment.

Risks Associated With This Offering

The offering price of our common stock will exceed the net tangible book value of our common stock after the offering.

Purchasers of securities in this offering will pay a much higher price than the book value of our common stock. The net tangible book value of our common stock immediately after this offering will be approximately \$0.28 per share, after giving effect to the sale of 15,252,040 shares of common stock in this offering at a public offering price of \$1.31 per share and without ascribing any portion of the offering price to the warrants included with the shares. Purchasers in this offering also may experience dilution upon the exercise of the warrants offered hereby, depending on our tangible net book value at the time of exercise.

We have broad discretion in how we use the proceeds of this offering, and we may use the proceeds in ways that do not enhance the value of our common stock.

Although we describe in the “Use of Proceeds” section in this prospectus supplement our currently intended use of the net proceeds of this offering, we will have significant flexibility in using the net proceeds. You will be relying on the judgment of our management and our board of directors with regard to the use of these net proceeds, and you will not have the opportunity, before making your investment decision, to assess whether the proceeds will be used appropriately. It is possible that our use of the net proceeds will not benefit our business or enhance the value of our common stock.

The exercise price of the warrants exceeds the market price of our common stock.

The warrants being offered in this offering will have an exercise price of \$1.70 per share of common stock, which exceeds the current and recent market prices of our common stock, and will expire on the fifth anniversary of their initial issuance. If the market price of our common stock does not exceed the exercise price of the warrants during the period in which the warrants are exercisable, the warrants may not have any value.

There is no public market for the warrants.

There is no established public trading market for the warrants being offered in this offering, and we do not expect a market to develop. In addition, we do not intend to apply for listing the warrants on any securities exchange or automated quotation system. Without an active market, purchasers in this offering may be unable to readily sell the

warrants.

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NOTE ON FORWARD-LOOKING STATEMENTS

Some of the statements contained or incorporated by reference in this prospectus supplement or in the accompanying prospectus may include forward-looking statements that reflect our current views with respect to our 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,” “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 in the “Risk Factors” sections of this prospectus supplement and the accompanying prospectus 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, 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 to 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 and in the accompanying prospectus that could cause actual results to differ.

USE OF PROCEEDS

We expect the net proceeds of this offering to be up to approximately \$18.3 million after deducting the placement agent fees and expenses described in the “Plan of Distribution” section in this prospectus supplement and other estimated offering expenses payable by us, which include financial advisory fees, accounting fees, legal fees, transfer agent fees and filing costs and various other fees associated with registering and listing the shares of common stock in this offering.

We intend to use the net proceeds of this offering for research and development, including clinical development of our lead product candidate, tamibarotene for the treatment of APL, and clinical and preclinical research and development with respect to other potential product candidates. We also intend to use the net proceeds for working capital and general corporate purposes, which may include our acquisition, in-licensing or investment in complementary products, product candidates, technologies or companies.

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 of this offering. Pending application of the net proceeds as described above, we intend to temporarily invest the net proceeds in short-term, interest-bearing securities.

DILUTION

If you purchase securities in this offering, you will experience dilution to the extent of the difference between the public offering price per share in this offering and the net tangible book value per share of our common stock immediately after this offering. As of March 31, 2009, our unaudited net tangible book value was approximately \$12.3 million, or approximately \$0.13 per share. Net tangible book value is total assets minus the sum of liabilities and intangible assets. Net tangible book value per share is net tangible book value divided by the total number of shares of our common stock outstanding.

Dilution per share to new investors 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 completion of this offering. After giving effect to the sale of 15,242,040 shares of our common stock being offered in this offering at a public offering price of \$1.31 per share and after deducting the placement agent fees and our estimated offering expenses, our as-adjusted net tangible book value as of March 31, 2009 would have been approximately \$30.6 million, or approximately \$0.28 per share, assuming no portion of the offering price is attributable to the warrants being offered in this offering. This amount represents an immediate increase in net tangible book value of \$0.15 per share to our existing stockholders and an immediate dilution of \$1.03 per share to purchasers in this offering, as illustrated in the following table:

Public offering price per share of common stock	\$1.31
Net tangible book value per share as of March 31, 2009	\$0.13
Increase in net tangible book value per share after giving effect to this offering	\$0.15
As-adjusted net tangible book value per share as of March 31, 2009 after giving effect to the offering	\$0.28
Dilution per share to new investors	\$1.03

Purchasers in this offering also may experience dilution upon the exercise of the warrants offered hereby, depending on our tangible net book value at the time of exercise.

The number of shares of our common stock used in the calculations above are based on 93,352,965 shares outstanding as of July 24, 2009, and excludes as of that date:

- 11,434,848 shares of our common stock issuable upon exercise of outstanding warrants at a weighted-average exercise price of \$1.32 per share;
- 7,061,847 shares of our common stock issuable upon exercise of outstanding stock options at a weighted-average exercise price of \$1.12 per share;
- 10,940,532 shares of common stock available for issuance with respect to future grants under our stock incentive plans;
- 3,813,010 shares of our common stock issuable upon the exercise of warrants to be issued to purchasers of this offering at an exercise price of \$1.70 per share; and
- 915,122 shares of common stock issuable upon exercise of the placement agent warrant to be issued in connection with this offering at an exercise price of \$1.70 per shares, which shares are not covered by this prospectus supplement.

The exercise of outstanding options and warrants having an exercise price less than the public offering price in this offering will increase dilution to purchasers in this offering.

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THE SECURITIES WE ARE OFFERING

In this offering we are offering to sell up to 15,252,040 shares of our common stock and warrants to purchase up to 3,813,010 shares of our common stock and to issue up to 3,813,010 shares of our common stock upon exercise of the warrants. The shares of common stock and the warrants will be issued separately. One Series A Junior Participating Preferred Stock Purchase Right that trades with our common stock will accompany each share of our common stock being offered.

The securities offered in this offering will be issued pursuant to a securities purchase agreement among the purchasers and us. You should review the securities purchase agreement and the form of the warrants, each of which have been filed by us as an exhibit to a Current Report on Form 8-K filed with the SEC in connection with this offering, for a complete description of the terms and conditions applicable to the securities we are offering. This description of the warrants in this prospectus supplement is qualified in its entirety by reference to the form of the warrants.

Common Stock

The material terms and provisions of our common stock and each other class of our securities which qualifies or limits our common stock are described under the caption "Description of Capital Stock" starting on page 31 of the accompanying prospectus. The shares of common stock issued in this offering will be, when issued and paid for in accordance with the securities purchase agreement, duly and validly authorized, issued and fully paid and non-assessable.

Warrants

The warrants to be issued in this offering represent the rights to purchase up to 3,813,010 shares of common stock at an initial exercise price of \$1.70 per share. Purchasers will receive a warrant to purchase 0.25 share of common stock for each share of common stock they purchase in this offering. Each warrant may be exercised at any time and from time to time on or after its original date of issuance (which we anticipate will occur not later than July 31, 2009) and through and including the fifth anniversary of the initial exercise date.

Exercise

Holders of the warrants may exercise their warrants to purchase shares of our common stock on or before the termination date by delivering (i) notice of exercise, appropriately completed and duly signed, and (ii) if such holder is not utilizing the cashless exercise provisions with respect to the warrants, payment of the exercise price for the number of shares with respect to which the warrant is being exercised. Warrants may be exercised in whole or in part, but only for full shares of common stock. Any portion of a warrant not exercised prior to the termination date shall automatically be exercised on the termination date by means of cashless exercise. We provide certain rescission and buy-in rights to a holder if we fail to deliver the shares of common stock underlying the warrants by the third trading day after the date on which delivery of the stock certificate is required by the warrant. With respect to the rescission rights, the holder has the right to rescind the exercise if stock certificates are not timely delivered. The buy-in rights apply if after the third trading day on which delivery of the stock certificate is required by the warrant, the holder purchases (in an open market transaction or otherwise) shares of our common stock to deliver in satisfaction of a sale by the holder of the warrant shares that the holder anticipated receiving from us upon exercise of the warrant. In this event, we will:

- pay in cash to the holder the amount equal to the excess (if any) of the buy-in price over the product of (A) such number of shares of Common Stock, times (B) the price at which the sell order giving rise to holder's purchase obligation was executed; and

- at the election of holder, either (A) reinstate the portion of the warrant as to such number of shares of common stock, or (B) deliver to the holder a certificate or certificates representing such number of shares of common stock.

In addition, the warrant holders are entitled to a “cashless exercise” option if, at any time of exercise, there is no effective registration statement registering, or no current prospectus available for, the issuance or resale of the shares of common stock underlying the warrants. This option entitles the warrant holders to elect to receive fewer shares of common stock without paying the cash exercise price. The number of shares to be issued would be determined by a formula based on the total number of shares with respect to which the warrant is being exercised, the volume weighted average of the prices per share of our common stock on the trading date immediately prior to the date of exercise and the applicable exercise price of the warrants.

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The shares of common stock issuable on exercise of the warrants will be, when issued and paid for in accordance with the warrants, duly and validly authorized, issued and fully paid and non-assessable.

Fundamental Transaction

If, at any time while the warrants are outstanding, we (1) consolidate or merge with or into another corporation, (2) sell all or substantially all of our assets, (3) are subject to or complete a tender or exchange offer pursuant to which holders of our common stock are permitted to tender or exchange their shares for other securities, cash or property, or (4) effect any reclassification of our common stock or any compulsory share exchange pursuant to which our common stock is converted into or exchanged for other securities, cash or property, each, a “Fundamental Transaction,” then the holder shall have the right thereafter to receive, upon exercise of the warrant, the same amount and kind of securities, cash or property as it would have been entitled to receive upon the occurrence of such Fundamental Transaction if it had been, immediately prior to such Fundamental Transaction, the holder of the number of warrant shares then issuable upon exercise of the warrant, and any additional consideration payable as part of the Fundamental Transaction. Any successor to us or surviving entity shall assume the obligations under the warrant.

Pro Rata Distributions, including Rights Offerings

If, at any time while the warrants are outstanding, we distribute evidences of our indebtedness, assets, or rights or warrants to purchase any security other than our common stock to all holders of our common stock, then the exercise price will adjust pursuant to a volume weighted average price based ratio, referred to as VWAP.

Certain Adjustments

The exercise price and the number of shares of common stock purchasable upon the exercise of the warrants are subject to adjustment upon the occurrence of specific events, including stock dividends, stock splits, combinations and reclassifications of our common stock.

Delivery of Certificates

Upon the holder’s exercise of a warrant, we will promptly, but in no event later than three trading days after the exercise date (the “Warrant Share Delivery Date”), issue and deliver, or cause to be issued and delivered, a certificate for the shares of common stock issuable upon exercise of the warrant. In addition, we will, if the holder provides the necessary information to us, issue and deliver the shares electronically through The Depository Trust Corporation through its Deposit Withdrawal Agent Commission System (DWAC) or another established clearing corporation performing similar functions. If we fail to deliver certificates evidencing the warrant shares by the Warrant Share Delivery Date, we are required to pay to the holder, in cash, as liquidated damages and not as a penalty, for each \$1,000 of warrant shares subject to such exercise (based on the VWAP of our common stock on the date of the applicable Notice of Exercise), \$2 per trading day (increasing to \$4 per trading day on the fifth trading day after such liquidated damages begin to accrue) for each trading day after such Warrant Share Delivery Date until such certificates are delivered or the holder rescinds such exercise.

Notice of Corporate Action

We will provide notice to holders of the warrants to provide them with the opportunity to exercise their warrants and hold common stock in order to participate in or vote on the following corporate events:

- if we shall take a record of the holders of our common stock for the purpose of entitling them to receive a dividend or other distribution, or any right to subscribe for or purchase any shares of stock of any class or any other right;

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- any capital reorganization of our company, any reclassification or recapitalization of our capital stock or any consolidation or merger with, or any sale, transfer or other disposition of all or substantially all of our property, assets or business to, another corporation; or
- a voluntary or involuntary dissolution, liquidation or winding up of our company.

Limitations on Exercise

The number of warrant shares that may be acquired by any holder upon any exercise of the warrant shall be limited to the extent necessary to insure that, following such exercise, the total number of shares of common stock then beneficially owned by such holder and its affiliates and any other persons whose beneficial ownership of common stock would be aggregated with the holder's for purposes of Section 13(d) of the Securities Exchange Act of 1934, does not exceed 4.99% of the total number of issued and outstanding shares of common stock (including for such purpose the shares of common stock issuable upon such exercise), or beneficial ownership limitation. The holder may elect to change this beneficial ownership limitation from 4.99% to 9.9% of the total number of issued and outstanding shares of common stock (including for such purpose the shares of common stock issuable upon such exercise) upon 61 days' prior written notice to us.

Additional Provisions

The above summary of certain terms and provisions of the warrants is qualified in its entirety by reference to the detailed provisions of the warrants, the form of which has been filed as an exhibit to a current report on Form 8-K that is incorporated by reference in the accompanying prospectus. We are not required to issue fractional shares upon the exercise of the warrants. No holders of the warrants will possess any rights as a stockholder under those warrants until the holder exercises those warrants. The warrants may be transferred independent of the common stock they were issued with, on a form of assignment, subject to all applicable laws.

We do not intend to list the warrants on any securities exchange or automated quotation system.

PLAN OF DISTRIBUTION

We have entered into a placement agency agreement, dated July 24, 2009, with Rodman & Renshaw, LLC. Subject to the terms and conditions contained in the placement agency agreement, the placement agent has agreed to act as exclusive placement agent in connection with the sale of up to 15,252,040 shares of our common stock and warrants to purchase up to 3,813,010 shares of our common stock in this offering. The placement agent is not purchasing or selling any securities by this prospectus supplement and the accompanying prospectus, nor is the placement agent required to arrange for the purchase or sale of any specific number or dollar amount of securities, but has agreed to use its reasonable best efforts to arrange for the sale of all of securities being offered in this offering.

The placement agency agreement provides that the obligations of the placement agent and the investors are subject to certain conditions precedent, including, among other things, the absence of any material adverse change in our business.

We currently anticipate that the closing of this offering will take place no later than July 31, 2009. On the closing date, the following will occur:

- we will receive funds in the amount of the aggregate purchase price of the shares sold;
- we will deliver the shares of our common stock and the warrants to the purchasers; and

- the placement agent will receive the placement agent fees and the placement agent warrants in accordance with the terms of the placement agency agreement.

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We have agreed to pay the placement agent an aggregate fee equal to 6% of the gross proceeds from the sale of the shares in this offering and to issue the placement agent a five-year warrant to purchase the number of shares of our common stock equal to 6% of the shares of our common stock sold in this offering, or 915,122 shares assuming all the shares of common stock offered hereby are sold, at an exercise price of \$1.70 per share, and to reimburse the placement agent for \$35,000 of expenses incurred by it in connection with this offering. We have also agreed to pay to each of our financial advisors, Brean Murray, Caret & Co., LLC, Natixis Bleichroeder, Inc., and Griffin Securities, Inc, an amount equal to two-thirds of 1% (or 2% in total) of such gross proceeds for advisory services rendered to us.

The placement agent warrants will be exercisable at the option of the holder at any time after the date of issuance, which will be the closing date of this offering, and through and including December 14, 2012, which is the date that is the fifth anniversary of the effective date of the registration statement relating to this offering. The exercise price of the placement agent warrants, and in some cases the number of shares issuable upon exercise of the warrants, will be subject to adjustment in the event of stock splits, stock dividends, combinations and similar events affecting our common stock. In addition, in the event we consummate a merger or consolidation with or into another person or other reorganization event in which our common stock is converted or exchanged for securities, cash or other property, or we sell, lease, license or otherwise dispose of all or substantially all of our assets or we or another person acquire 50% or more of our outstanding common stock, then following such event, the holders of the placement agent warrants will be entitled to receive upon exercise of the warrants the same kind and amount of securities, cash or property which the holders would have received had they exercised the placement agent warrants immediately prior to such fundamental transaction. Our successor or the surviving entity in such a transaction must assume the obligations under the placement agent warrants. In certain circumstances, the placement agent warrants may be exercised on a “net” or “cashless” basis.

The estimated offering expenses payable by us, in addition to the aggregate fees and expenses of approximately \$1.25 million due the placement agent, are approximately \$0.5 million, which includes financial advisory fees, legal fees, accounting fees, transfer agent fees and filing costs and various other fees associated with registering and listing the shares of common stock. After deducting fees due to the placement agent and our estimated offering expenses, we expect the net proceeds from this offering to be approximately \$18.3 million.

The following table shows the per share and total fees we will pay to the placement agent in connection with the sale of the shares of common stock and the warrants offered pursuant to this prospectus supplement and the accompanying prospectus, assuming the purchase of all of the shares of common stock and warrants offered hereby:

Per share placement agent fee	\$0.08
Maximum total offering total	\$1,200,000

We have agreed to indemnify the placement agent and certain other persons against certain liabilities relating to or arising out of the placement agent’s activities under the placement agency agreement. We have also agreed to contribute to payments the placement agent may be required to make in respect of such liabilities.

The placement agent has informed us that it will not engage in over allotment, stabilizing transactions or syndicate covering transactions in connection with this offering.

The purchase price of the shares of common stock and terms of the warrants were determined by us based on negotiations with the investors and discussions with the placement agent.

LEGAL MATTERS

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TroyGould PC, Los Angeles, California, has passed on the validity of the securities being offered hereby. As of July 24, 2009, TroyGould PC owned 70,000 shares of our common stock and warrants to purchase 7,146 shares of our common stock, as well as 23,491 shares of common stock of RXi. The placement agent is being represented in connection with this offering by Weinstein Smith LLP, New York, New York.

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EXPERTS

The consolidated financial statements, schedule and management's report on the effectiveness of internal control over financial reporting incorporated by reference in the accompanying prospectus have been audited by BDO Seidman, LLP, an independent registered public accounting firm, to the extent and for the periods set forth in their reports incorporated herein by reference, and are incorporated herein in reliance upon such reports given upon the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the informational requirements of the Securities Exchange Act of 1934, or the Exchange Act, and are required to file annual, quarterly and other reports, proxy statements and other information with the SEC. You may inspect and copy these reports, proxy statements and other information at the public reference facilities maintained by the SEC in Washington, D.C. (100 F Street NE, Room 1580, Washington, D.C. 20549). Copies of such materials can be obtained from the SEC's public reference section at prescribed rates. You may obtain information on the operation of the public reference rooms by calling the SEC at (800) SEC-0330 or on the SEC website located at <http://www.sec.gov>.

Our common stock is traded on the Nasdaq Capital Market under the symbol "CYTR." Reports, proxy and information statements and other information concerning us also may be inspected at the offices of the National Association of Securities Dealers, Inc. located at 1735 K Street, N.W., Washington, D.C. 20006.

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

PROSPECTUS

CYTRX CORPORATION

\$100,000,000

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

We will provide the specific terms of these offers and sales in supplements to this prospectus. This prospectus may not be used to sell securities unless accompanied by a prospectus supplement. You should read this prospectus and the 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 July 9, 2009, the last sale price of our common stock as reported on the Nasdaq Capital Market was \$1.00.

An investment in our securities involves a high degree of risk. Before purchasing any securities, you should consider carefully the risks referred to under "Risk Factors" on page 16 in this prospectus and in the prospectus supplement.

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

THE DATE OF THIS PROSPECTUS IS JULY 23, 2009

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ABOUT THIS PROSPECTUS

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

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

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

You should rely only on the information provided in this prospectus and in the prospectus supplement, including any information incorporated by reference. For more details on information incorporated herein by reference, you should review the discussion contained under the heading “Incorporation of Information Filed With the SEC.” 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.

In this prospectus, we sometimes refer to CytRx Corporation as “CytRx,” to our former subsidiary, RXi Pharmaceuticals Corporation, as “RXi,” and to Innovive Pharmaceuticals, Inc., which we acquired in September 2008, as “Innovive.” References in this prospectus and the prospectus supplement to “we,” “us,” “our” or the “company” refer to CytRx alone.

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” 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 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, all of which you should review carefully. Please consider our forward-looking statements in light of those risks as you read this prospectus and the prospectus supplement. We undertake no obligation to publicly update or review any forward-looking statement, whether as a result of new information, future developments or otherwise.

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

DESCRIPTION OF OUR BUSINESS

General

We are a biopharmaceutical research and development company engaged in the development of high-value human therapeutics. Our drug development pipeline includes two product candidates in clinical development for cancer indications, including registration studies of tamibarotene for the treatment of acute promyelocytic leukemia, or APL. In addition to our core oncology programs, we are developing treatments for neurodegenerative and other disorders based upon our small-molecule molecular chaperone amplification technology. We also have been engaged in new-drug discovery research at our laboratory facility in San Diego, California, utilizing our master chaperone regulator assay, or MaCRA, technology. In May 2009, we substantially completed the initial phase of these activities, and announced that we will conduct our research and development activities through third parties for the foreseeable future. Apart from our drug development programs, we maintain at present a 45% equity interest in our former subsidiary, RXi Pharmaceuticals Corporation, or RXi (NASDAQ: RXII).

On September 19, 2008, we completed the merger acquisition of Innovive Pharmaceuticals, Inc., or Innovive, and its clinical-stage oncology product candidates, including tamibarotene. As a result of the merger, Innovive became our wholly owned subsidiary. On December 30, 2008, we merged the former Innovive subsidiary into CytRx. Prior to our acquisition of Innovive, we were focused on developing human therapeutics based primarily upon our small-molecule molecular chaperone amplification technology, including arimoclomol for amyotrophic lateral sclerosis, which is commonly known as ALS or Lou Gehrig's disease, and iroxanadine for diabetic foot ulcers and other potential indications. After acquiring Innovive, we redirected our efforts to developing Innovive's lead oncology product candidates, tamibarotene for APL, INNO-206 for small cell lung cancer, or SCLC, and other solid tumor cancers, and bafetinib, which we believe hold greater near-term revenue potential than our molecular chaperone product candidates. Our current business strategy is to seek one or more strategic partnerships for the further development of arimoclomol and iroxanadine.

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 Product Candidate Pipeline

The following tables summarize the current pipeline of our product candidates:

Technology	Product candidate	Indication	Stage of development
Synthetic retinoid	Tamibarotene	APL (acute promyelocytic leukemia)	Pivotal Phase II
Doxorubicin prodrug	INNO-206	SCLC (small cell lung cancer) and other solid tumor cancers	Phase II (2H-2009)
Tyrosine kinase inhibitor	Bafetinib (formerly INNO-406)	CML (chronic myeloid leukemia)	Phase I
Molecular chaperone amplification	Arimoclomol	ALS (amyotrophic lateral sclerosis, or Lou Gehrig's disease) and stroke recovery	Phase IIb
Molecular chaperone amplification	Iroxanadine	Diabetic foot ulcers, other indications	Phase I

Our Clinical Development Programs

Our current clinical development programs consist of our efforts to develop tamibarotene for APL and INNO-206 for SCLC or other solid tumor types and our planned animal toxicology studies designed to facilitate a Phase IIb clinical study of arimoclomol in ALS, which has been placed on hold by the United States Food and Drug Administration, or FDA.

Tamibarotene. Tamibarotene is a synthetic retinoid designed to overcome resistance and avoid toxic side effects of differentiation therapy with all-trans retinoic acid, or ATRA, a component of the current first-line treatment for APL.

Tamibarotene for the treatment of APL. Acute promyelocytic leukemia, or APL, is a specific type of acute myeloid leukemia characterized by the t(15;17) translocation, which fuses the promyelocytic leukemia, or PML, gene on chromosome 15 to the retinoic acid receptor, or RAR, α gene on chromosome 17. This fusion causes abnormal cell growth.

Differentiation therapy with ATRA, is the basis for the treatment of APL. Differentiation therapy causes leukemic promyelocytes to mature and undergo cell death. Patients typically receive ATRA in combination with chemotherapy as the initial therapy, followed by anthracycline-based consolidation therapy designed to produce complete remission. The majority of patients treated this way generally experience a complete remission of disease. Current National Comprehensive Cancer Network guidelines recommend that patients then undergo one to two years of maintenance therapy with ATRA to prevent a recurrence. ATRA therapy is associated with several toxicities, the most serious of which, retinoic acid syndrome, or RAS. RAS occurs in up to 25% of patients treated with ATRA, a serious and potentially fatal complication characterized by fever, dyspnea (breathing difficulties), weight gain, pulmonary infiltrates (abnormal accumulation in the lungs), and pleural or pericardial effusions (excess fluid around the lungs or heart).

Patients that initially respond to front-line therapy with ATRA plus chemotherapy sometimes relapse, and some of these patients fail to respond to a second course of treatment with ATRA. Currently, patients who fail ATRA-based therapy are treated with arsenic trioxide, a compound administered intravenously and associated with significant toxicity, including irregular heartbeat. There currently is no standard of care for patients who do not respond to ATRA and arsenic trioxide, or who respond but subsequently relapse. In 2007, the FDA granted Orphan Drug Designation and Fast Track Designation for the use of tamibarotene in patients with relapsed or refractory APL following treatment with ATRA and arsenic trioxide.

Tamibarotene was developed to overcome resistance to ATRA. In vitro, tamibarotene is approximately ten times more potent than ATRA at causing APL cells to differentiate and die. In addition, tamibarotene has a lower affinity for cellular retinoic acid binding protein, or CRABP, which we believe should allow for sustained plasma levels during administration. This may enhance tamibarotene's potential efficacy, because patients may be able to experience benefits from the drug over a longer period of time. Tamibarotene does not bind the RAR- γ receptor, the major retinoic acid receptor in the dermal epithelium, which should lessen the occurrence of RAS. In clinical studies, the rate of RAS appeared to be low.

Pre-clinical data. In a variety of preclinical models, tamibarotene was superior to ATRA in its ability to cause APL cells to differentiate and die. In the clinical setting, in vitro response to tamibarotene appeared predictive of clinical response, including activity in patients who had a poor response to ATRA.

Clinical data. Tamibarotene is approved in Japan under the brand name Amnolake for use in relapsed or refractory APL. The approval was based on data from two studies in Japanese patients. In the pivotal study, the effectiveness of orally administered tamibarotene was evaluated in 39 patients with APL, including patients who had never received treatment for APL and patients who had been previously treated with ATRA. Tamibarotene was administered orally at a dose of 6 mg/m²/day for eight weeks. The overall complete response rate in these patients was 61.5%. In patients who had a recurrence of APL following ATRA therapy, the response rate was 81%. RAS was reported in three patients, or 7.3% of the patient group.

Development Plan. We re-initiated a pivotal study in ATRA and arsenic trioxide refractory APL in the second quarter of 2008. The study is designed to collect pharmacokinetic, safety and efficacy data in approximately 50 patients.

Depending on its outcome, this study, in combination with the data from the two Japanese studies, would form the basis of a new drug application, or NDA. If the results of the study are positive, and if we are able to manufacture tamibarotene in commercial quantities in compliance with stringent regulatory requirements, we believe that we would be able to file the NDA with the FDA in 2011.

In addition, a Phase III study is currently being conducted in Japan by the Japan Adult Leukemia Group comparing ATRA to tamibarotene for the maintenance treatment of APL. If positive, these data could potentially form the basis of a supplemental NDA application.

INNO-206. INNO-206 (formerly DOXO-EMCH) is a prodrug for doxorubicin. Specifically, it is the (6-Maleimidocaproyl) hydrazone of doxorubicin. Essentially, this chemical is doxorubicin (DOXO) attached to an acid sensitive linker (EMCH).

INNO-206 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 digestive tract, including the mouth), stomatitis (inflammation of the mouth's soft tissue), and extravasation (the leakage of intravenous drugs from the vein into the surrounding tissue).

We believe INNO-206 has attributes that improve on native doxorubicin, including reduction of adverse events, improvement in efficacy and the ability to reach the tumor more quickly.

Our anticipated mechanism of action for INNO-206 is as follows:

- after administration, INNO-206 rapidly binds endogenous circulating albumin through the EMCH linker;
- circulating albumin preferentially accumulates in tumors, bypassing uptake by other non-specific sites, including the heart, bone marrow and the gastrointestinal tract;
- once albumin-bound INNO-206 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.

Pre-clinical data. In a variety of preclinical models, INNO-206 was superior to doxorubicin in its ability to increase dosing, antitumor efficacy, and safety, including a reduction in cardiotoxicity.

Clinical data. A Phase I study of INNO-206 that demonstrated safety and objective clinical responses in a variety of tumor types was completed in 2005 and presented at the March 2006 Krebskongress meeting in Berlin. In this study, single doses were administered at up to six times the standard dosing of doxorubicin without an increase in observed side effects over historically observed levels with doxorubicin. Twenty-four of 35 evaluable patients had either a clinical response or stable disease. Objective clinical responses were observed in patients with sarcoma, breast, and lung cancers.

Development Plan. Based on the objective clinical responses seen in the Phase I study, we intend to initially develop INNO-206 as a therapeutic for patients with solid tumors, such as SCLC patients who have relapsed after initial chemotherapy. This indication has a very poor prognosis with the current standard of care, topotecan, which is used in approximately 30% of SCLC patients. Based on the existing preclinical and clinical data for INNO-206, we believe there is the potential to demonstrate superiority to topotecan in the second-line SCLC setting.

Beyond this initial indication, we will explore the utility of INNO-206 in chemotherapy regimens that currently include doxorubicin, both for solid tumors and other indications. If the Phase I data were to hold up in larger randomized studies, we believe the potential exists for INNO-206 to replace doxorubicin based on higher efficacy and improved side effect profile, although this has not been proven.

Bafetinib. Bafetinib (formerly INNO-406) is a novel drug developed by the Japanese pharmaceutical company Nippon Shinyaku, to overcome the limitations of Gleevec and second-line tyrosine kinase inhibitors in resistant chronic myelogenous leukemia, or CML. At present, there are no approved third-line treatments for refractory CML.

Bafetinib for the Treatment of CML. CML is a type of blood cancer that occurs in approximately 4,570 patients per year in the U.S. Approximately 95% of CMLs contain a genetic translocation known as Bcr-Abl, which signals the cells to proliferate. Bcr-Abl does not exist in normal cells.

In 2001, Novartis AG won approval in the U.S. for its drug, Gleevec. Gleevec is a chemical molecule specifically designed to stop Bcr-Abl from emitting its signals for cell growth. Gleevec proved effective in treating patients with CML by inhibiting Bcr-Abl. Patients remain on Gleevec as chronic therapy. The reported five-year survival rate for patients with CML has gone from approximately 35% before the approval of Gleevec in 2001 to approximately 90% in 2006. Worldwide sales of Gleevec in 2006 were \$2.5 billion.

Unfortunately, resistance to Gleevec has begun to occur. Resistance to Gleevec appears to occur due to amplification of the Bcr-Abl gene and, in many cases, mutations in the Bcr-Abl gene. In other cases, some of the genes that Bcr-Abl signals to turn on are becoming turned on independently of Bcr-Abl, making inhibition of the gene by Gleevec ineffective. Lyn is a member of the Src family of kinases. These kinases are known to be involved in sending out signals that drive cell growth. Lyn has been shown to be one of the genes that is turned on by Bcr-Abl, and Lyn is known to be active in some Gleevec-resistant CMLs. Activation of Lyn is therefore suspected of being another mechanism by which cells become resistant to Gleevec.

The development of resistance to Gleevec means that a second generation of drugs is required to treat CML. Ideally, these new drugs would be able to inhibit Bcr-Abl, even in its mutated form, and also independently turn off other genes that Bcr-Abl normally activates.

Dasatinib, from Bristol-Myers Squibb, is the leading second-generation Bcr-Abl inhibitor. Dasatinib gained conditional U.S. marketing approval in June 2006. Dasatinib has high potency in inhibiting Bcr-Abl and also inhibits Src, a family of kinases known to be involved in cell growth. In clinical studies, Dasatinib has shown good activity in Gleevec-resistant patients. However, there have also been concomitant side effects, including serious and life-threatening pleural effusion. In fact, it is estimated that two-thirds of patients experience dose reductions or interruptions, and in data provided by Bristol-Myers Squibb 20% to 30% of patients that initiate dasatinib therapy discontinue its use due to intolerance. This side effect profile is believed to be due to non-specific kinase inhibition, but that has not yet been proven. It is not clear whether a Bcr-Abl and Lyn inhibitor would have similar side effects.

Nilotinib, another second generation Bcr-Abl inhibitor being developed by Novartis AG, received accelerated approval in the U.S. Nilotinib has potent activity against Bcr-Abl. In its Phase I clinical trial, Nilotinib showed good activity in Gleevec-resistant patients. In Phase II clinical data presented at the American Society for Hematology conference in 2006, Nilotinib showed efficacy similar to dasatinib in Gleevec-resistant patients.

Bafetinib is roughly 25 to 55 times more potent at inhibiting Bcr-Abl than Gleevec in cell culture. Bafetinib is also capable of inhibiting 19 of the 20 tested mutated forms of Bcr-Abl in CML that are resistant to Gleevec. In addition, bafetinib is capable of shutting down the activity of the Lyn protein. This ability to inhibit the activity of Lyn is independent of bafetinib's ability to inhibit Bcr-Abl.

We believe that these properties of bafetinib, including its higher potency than Gleevec, the ability to inhibit the mutated forms of Bcr-Abl and the addition of Lyn inhibition, might make it an effective treatment for CML, although we are in the early stages of the clinical testing only and none of bafetinib's potential advantages have been clinically proven.

Pre-clinical Data. In mice-leukemia models, bafetinib has been shown to markedly extend the survival of animals implanted with Gleevec-resistant leukemic cells. In toxicology studies done in mice, rats, and dogs, bafetinib appeared to be safe and well-tolerated. A dose was described in dogs in which no side effects were seen was used to calculate the starting dose in humans for our recently completed clinical trial.

Phase I Study. In November 2008, we announced that bafetinib demonstrated clinical responses in patients with CML in a Phase I clinical trial conducted in patients with CML and other leukemias that have a certain mutation called the Philadelphia Chromosome (Ph+) and are intolerant of or resistant to Gleevec and, in some cases, second-line tyrosine kinase inhibitors such as dasatinib (Sprycel®) and nilotinib (Tasigna®). The clinical trial was designed to identify the optimal dose for possible future studies by escalating doses from 30 mg once per day to up to 480 mg twice per day in a total of 56 patients with Ph+ leukemias. Of the patients, 31 had CML in chronic phase (CML-CP), nine were in accelerated phase (CML-AP), seven were in blast phase (CML-BP), and nine had Ph+ acute lymphocytic leukemia. The clinical trial was conducted at seven clinical sites in the US, Germany, and Israel, with Hagop Kantarjian, M.D., Professor & Chairman, Department of Leukemia, The University of Texas, M.D. Anderson Cancer Center, serving as the Principal Investigator. A positive, dramatic decrease in the number of leukemia cells in the bone marrow was seen in 35% of the patients that were randomly chosen to begin their treatment with the optimal INNO-406 dose of 240 mg twice per day.

The maximum tolerated dose was determined to be 240 mg given twice per day, based on evidence of increasing potential liver toxicity at higher doses. Common adverse events (observed in greater than 20% of patients in the 240 mg twice per day dose group) were gastrointestinal related, swelling, and fatigue. There was no evidence of fluid accumulating around the lungs, or significant changes in a certain heart rhythm called QTc prolongation, which are serious side effects known to occur in patients treated with approved drugs for this indication. Approximately 13% of patients across all dose groups discontinued dosing due to unacceptable toxicity.

In 2007, the FDA granted Orphan Drug Designation to bafetinib for the treatment of Gleevec-resistant or intolerant CML. Based on the results of our Phase I study, we intend to seek a strategic partner for the further development of bafetinib.

Arimoclomol. Arimoclomol is an orally-administered small-molecule product candidate that we believe functions by stimulating a normal cellular protein repair pathway by amplifying activated molecular chaperone proteins implicated in neurological disorders.

Arimoclomol for the treatment of ALS. ALS, or Lou Gehrig's disease, is a debilitating and ultimately deadly disease involving the progressive degeneration of motor neurons believed to be caused by toxic mis-folding of proteins. According to the ALS Association, approximately 30,000 people in the U.S. are living with ALS and 5,600 new cases are diagnosed each year. Worldwide, an estimated 120,000 people are living with ALS. According to the ALS Survival Guide, 50% of ALS patients die within 18 months of diagnosis and 80% die within five years of diagnosis.

The following is a summary of our clinical development of arimoclomol for treating ALS:

- in July 2006, we completed an 84-patient, multi-center, double-blind, placebo-controlled, multi-dose Phase IIa clinical trial of safety and tolerability of arimoclomol in volunteers with ALS, which we refer to as the Phase IIa trial;
- in May 2007, we completed an open-label extension of the Phase IIa trial in approximately 70 ALS patients from the trial who were administered the highest investigational dose (100 mg three times daily) of arimoclomol for an additional six months;
- in June 2007, we completed a multiple ascending-dose clinical trial of safety and tolerability involving 40 healthy volunteers;
- in November 2007, we completed a 28-day safety clinical trial with 400 mg of arimoclomol three times daily involving 16 healthy volunteers; and

- in December 2007, we initiated patient screening in a double blind, placebo-controlled Phase IIb clinical study. In this trial, we expect to enroll 390 ALS patients at 30 to 40 clinical sites in the U.S. and Canada. The primary purpose of this trial is to evaluate the safety and efficacy of a 400 mg dose of arimoclomol administered orally three times daily. The Phase IIb clinical trial was placed on clinical hold by the FDA in January 2008. Based on written correspondence we received from the FDA, their decision pertained to a previously completed animal toxicology study in rats and was not related to data generated from any human studies with arimoclomol. We have completed additional animal toxicology studies to obtain additional safety data that we submitted to the FDA in the second quarter of 2009.

Phase IIa clinical trial. Participants in the Phase IIa clinical trial of arimoclomol were administered either a placebo capsule, or one of three dosage levels of arimoclomol capsules, three times daily for a period of 12 weeks, immediately followed by a one-month period without the drug. The primary endpoints of the Phase IIa trial were safety and tolerability. Secondary endpoints included a preliminary evaluation of efficacy using two widely accepted disease-progression markers. The first marker, the revised ALS Functional Rating Scale, or ALSFRS-R, is used to determine patients' overall functional capacity and independence in 13 activities. The second marker measures vital capacity, an assessment of lung capacity, which is an important disease indicator since ALS sufferers eventually lose the ability to breathe on their own. The trial was designed to be able to detect only extreme responses in these two markers.

The results from our Phase IIa trial and open-label extension clinical trial indicated that arimoclomol was safe and well tolerated in ALS volunteers, even at the highest administered dose. Arimoclomol was detected in participants' cerebral spinal fluid, demonstrating that it passed the so-called blood:brain barrier, and participants treated with arimoclomol experienced a statistically significant decrease in adverse events of weakness compared with the placebo group. As would be expected based upon the small size and short duration of the Phase IIa trial, we observed no statistically significant effects in disease progression markers. We did, however, observe a trend toward slower disease progression in the highest dosage group. Since there was no concurrent placebo control group in our open-label extension clinical trial, we compared the results with results in an untreated placebo group with similar characteristics in a prior ALS clinical trial published in July 2006 in *Annals of Neurology*. The results indicated a trend toward a slower average progression in every disease marker in the patients treated with arimoclomol compared to the historical placebo control. In particular, we observed a decrease of 21% in the rate of decline for ALSFRS-R, 8% for vital capacity, 23% for total body weight and 20% for body mass index when compared with that historical control. No definitive conclusions can be drawn from these data without a concurrent placebo control group, and investors are cautioned against relying on these data as an indication of arimoclomol's potential efficacy.

The favorable safety and tolerability profile observed in our Phase IIa trial, open-label extension clinical trial and animal toxicology studies of arimoclomol suggested that we may be able to safely increase the dose of arimoclomol without causing significant side effects. The results from the subsequent multiple ascending-dose study indicated that arimoclomol was safe and well tolerated, even at doses of 600 mg three times daily (six times higher than the highest dose used in the Phase IIa and open-label studies), when administered to healthy volunteers over a seven-day period. Results from the 28-day safety clinical trial in healthy volunteers indicated that the dosage of 400 mg administered three times daily also was safe and well tolerated.

Phase IIb efficacy trial. In January 2008, the FDA placed on clinical hold our planned efficacy trial to evaluate the safety and efficacy in ALS patients of a 400 mg dose of arimoclomol administered orally three times daily. Based on written correspondence we received from the FDA, their decision pertained to a previously completed animal toxicology study in rats and was not related to data generated from any human studies with arimoclomol. We have completed additional animal toxicology studies to obtain additional safety data that we submitted to the FDA in the second quarter of 2009. We plan to seek a strategic partner for the further development of arimoclomol for all indications.

Other Clinical Development. In February 2009, a Phase II/III adaptive clinical trial commenced to study arimoclomol in a subset of patients with the inherited or familial form ALS. Patients with familial ALS (fALS) who harbor certain mutations in the superoxide dismutase-1 (SOD1) gene suffer from a rapidly progressing form of the disease. The clinical trial is being financially supported by grants from the ALS Association and the U.S. Food and Drug Administration's (FDA's) Office of Orphan Products Development (OOPD), and we are supplying the drug and allowing the sponsor to reference our Investigational New Drug Application for regulatory purposes.

Arimoclomol for recovery from stroke. Stroke results from an acute loss of normal blood flow to the brain caused most often by a blockage in a blood vessel (ischemic) or due to leaking of blood from a vessel (hemorrhagic). According to the American Heart Association: stroke is the third leading cause of death and the number one cause of long-term disability in the U.S.; between 50% and 70% of stroke survivors regain functional independence, but between 15% and 30% are permanently disabled and 20% require institutional care within three months after stroke; and the direct and indirect stroke cost in the U.S. totaled approximately \$58 billion in 2006.

After the normal flow of blood is restored to the brain after the initial event, post-stroke neurological function continues to decline. We believe that this continuing decline in neurological function is the consequence of mis-folded protein aggregates generated as a result of oxygen deprivation during the original event.

Preclinical efficacy studies completed by us in April 2007 indicated that arimoclomol accelerated the time to recovery, and improved recovery, in experimental animal models of stroke. These results were obtained even when arimoclomol was administered as long as 48 hours after onset.

By comparison, tissue plasminogen activator, or t-PA, the only treatment currently approved in the U.S. for acute ischemic stroke, must be administered within three hours of stroke, which substantially limits the number of patients who qualify for this treatment.

In light of these preclinical data, we plan to seek a partner for the development of arimoclomol for stroke recovery and other indications.

Iroxanadine. Iroxanadine also is an orally-administered small-molecule product candidate. We believe it functions by stimulating the molecular chaperone protein response in the endothelium, the thin layer of cells that line the interior surface of human blood vessels.

Iroxanadine for the treatment of diabetic ulcers. Type 2 diabetes is a major health problem with significant secondary complications. The American Diabetes Association estimates that there are 21 million type 2 diabetes sufferers in the U.S. The World Health Organization estimates that there are more than 162 million cases of type 2 diabetes worldwide. According to the American Diabetes Association, 15% of all diabetics will develop a foot ulcer during their lifetime, and over 82,000 non-traumatic lower-limb amputations were performed on diabetics in the U.S. in 2002 due to such ulcers and other complications. We believe there is strong support in the scientific literature for the assertion that diabetic foot ulcers fail to heal efficiently, in part, due to the dysfunction of endothelial cells lining the blood vessels caused by protein mis-folding.

Animal studies completed by us in May 2007 indicated that iroxanadine significantly decreased the time it took for wounds to heal in diabetic mice without affecting healing in healthy mice. Wound healing in the diabetic mice, which normally required twice the time to heal as healthy mice, was accelerated to the extent that healing time of diabetic mice treated with iroxanadine was indistinguishable from that in untreated healthy mice.

In Phase I clinical trials in healthy volunteers and Phase II clinical trials in patients with chronic high blood pressure conducted prior to our acquisition of iroxanadine, iroxanadine was determined to be safe and well-tolerated and demonstrated significant improvement in the function of endothelial cells in the brachial artery, a major blood vessel of the upper arm.

Based on our preclinical results and the earlier clinical study data, we plan to seek a strategic partner for the further development of iroxanadine.

Our New-Drug Discovery Research Programs and Other Technologies

We are conducting research aimed at discovering and validating novel drug targets utilizing our master chaperone regulator assay, or MaCRA, drug discovery process. We have filed a patent application on our MaCRA technology and on new chemical entities discovered in the laboratory. We continue to assess periodically the costs and potential commercial value of our new-drug discovery activities, and recently announced that we would conduct any further activities through third party research.

Our other current technologies, which we developed prior to the acquisition of our molecular chaperone amplification technology, are CRL-5861, an intravenous agent for treatment of sickle cell disease and other acute vaso-occlusive disorders, and TranzFect, a delivery technology for DNA-based and conventional vaccines and other potential uses.

Our Separation from RXi Pharmaceuticals Corporation

Until early 2008, we owned approximately 85% of the outstanding shares of common stock of RXi and our financial statements, including our financial statements as of and for the year ended December 31, 2007, included the consolidated financial condition and results of operations of RXi. On February 14, 2008, our board of directors declared a dividend of one share of RXi common stock for each approximately 20.05 outstanding shares of our common stock, which was paid on March 11, 2008 and which reduced our ownership of RXi shares to less than 50%. As a result, our financial statements since March 11, 2008 no longer consolidate the financial condition and results of operation of RXi, but instead reflect our ongoing investment in RXi based on the equity method of accounting. As of July 8, 2009, we owned approximately 45% of the outstanding shares of RXi common stock.

We are party to a letter agreement with RXi and some of RXi's current stockholders under which we are entitled to preemptive rights to acquire any "new securities" (as defined) that RXi proposes to sell or issue, so that we may maintain our percentage ownership in RXi. Our preemptive rights will expire on January 8, 2012 or such earlier time at which we own less than 10% of RXi's outstanding common stock.

Under the letter agreement with RXi, we agreed to vote our RXi shares for the election of RXi directors and take other actions to ensure that a majority of the board of directors of RXi are independent of us. We further agreed to approve of actions that may be adopted and recommended by the RXi board of directors to facilitate any future financing by RXi.

Manufacturing

We have no capability to manufacture supplies of any of our products, and rely on third-party manufacturers to produce materials needed for research and clinical trials. We have contracted with various contract manufacturing facilities for supply of our active pharmaceutical ingredient, or API, for our product candidates. Pursuant to our license with TMRC Co., Ltd., or TMRC, relating to tamibarotene, TMRC will provide us with tamibarotene at a fixed price and in a quantity and quality sufficient to meet our clinical and commercial needs.

To be commercialized, our products also must be capable of being manufactured in commercial quantities in compliance with stringent regulatory requirements and at an acceptable cost. We intend to rely on third-party manufacturers to produce commercial quantities of any products for which we are able to obtain marketing approval. We have not commercialized any product, and so we also have not demonstrated that any of our product candidates can be manufactured in commercial quantities in accordance with regulatory requirements or at an acceptable cost.

If our 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 our products are not able to be manufactured at an acceptable cost, the commercial success of our products may be adversely affected.

Marketing

Our tentative plan is to establish our own sales force and marketing capability in order to commercialize tamibarotene and INNO-206 in the U.S. and to seek a marketing partner for commercialization in 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 acquired patents and patent applications, and have filed several new patent applications, in connection with our molecular chaperone program.

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 molecular chaperone amplification and other small molecule technology or other 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.

License Agreements

Tamibarotene

We have succeeded to Innovive's agreement with TMRC for the license of patent rights held by TMRC for the North American development and commercialization of tamibarotene. The license is exclusive, applies to all products that may be subject to the licensed intellectual property and may be used in the treatment of APL. We may sublicense the intellectual property in our sole discretion. The agreement also grants us an option to include within the license the use of the drug in other fields in oncology including multiple myeloma, myelodysplastic syndrome, and solid tumors.

Under the agreement, we must pay TMRC royalties based on net sales and make payments to TMRC in the aggregate of \$4.165 million upon meeting clinical, regulatory, and sales milestones up to and including the first commercial sale of the product for the treatment of APL.

Under the agreement, we must use commercially reasonable efforts to conduct the research and development activities we determine are necessary to obtain regulatory approval to market the product in those countries in North America that we determine are commercially feasible.

The agreement will expire upon the expiration of the subject patent rights, or 15 years from the date of first commercial sale of product in North America, whichever is later. The agreement may be terminated if either party is in breach and the breach is not cured within a required amount of time. We may also terminate the agreement in the event of a material change in the safety profile of the technology that makes continued development impossible.

INNO-206

We also have succeeded to Innovive's agreement with KTB Tumorforschungs GmbH, or KTB, for the license of patent rights held by KTB for the worldwide development and commercialization of INNO-206. The license is exclusive and worldwide, applies to all product that may be subject to the licensed intellectual property and may be used in all fields of use. We may sublicense the intellectual property in our sole discretion. The agreement also grants us an option to include within the license any technology that is claimed or disclosed in the licensed patents and patent applications for use in the field of oncology and the right of first refusal on any license that KTB wishes to make to a third party regarding any 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 \$7.5 million upon meeting clinical and regulatory milestones 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 non-royalty sub-licensing income (as defined in the agreement); and

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

In the event that we must pay a third party in order to exercise our rights to the intellectual property under the agreement, we will deduct a percentage of those payments from the royalties due KTB, up to an agreed upon cap. This deduction includes a percentage of any payments that might be required to be made by us to Bristol-Myers Squibb. Bristol-Myers Squibb holds a patent on technology that might be considered to block the patents and patent applications that are the subject of the agreement with KTB.

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 the product 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 API of the product 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.

Bafetinib

We likewise have succeeded to Innovive's exclusive, worldwide (with the exception of Japan) royalty-bearing license agreement with Nippon Shinyaku, including the right to grant sublicenses, for the intellectual property relating to bafetinib in all fields. The license agreement will expire on a country-by-country basis upon the expiration of the subject patent rights. The bafetinib license covers two Patent Cooperation Treaty, or PTC, applications filed in 2003 and 2004, respectively.

Under the agreement, we are obliged to pay Nippon Shinyaku an aggregate of \$13.35 million (including \$5 million upon the product's initial final marketing approval) upon the achievement of clinical and regulatory milestones up to and including approvals in the U.S. and Europe. We also will be obliged to pay:

- commercially reasonable royalties based on a percentage of net sales (as defined in the Nippon Shinyaku license 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 license agreement).

The agreement includes covenants that require us to, among other things, file an NDA by a specific date and use our commercially reasonable efforts to bring a licensed product to market. In the event that we breach a material term of the Nippon Shinyaku license agreement, Nippon Shinyaku has the option to terminate the agreement following the giving of notice and an opportunity to cure any such breach.

Under the merger agreement by which we acquired Innovive, we agreed to pay the former Innovive stockholders up to \$1.01 per Innovive share 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.

Competition

To our knowledge, there are no competitors in clinical development for refractory APL. Currently, treatment of APL is based on induction and maintenance therapy with ATRA and chemotherapy (typically idarubicin). ATRA and idarubicin are both generic compounds. Arsenic trioxide, currently marketed by Cephalon, is approved for use in patients who have relapsed after ATRA-based therapy in APL. There are no FDA-approved therapies for patients who have failed arsenic trioxide. In practice, it appears that patients who fail arsenic trioxide are retreated with ATRA or receive Mylotarg, which is marketed by Wyeth Pharmaceuticals.

We are aware of two compounds in late-stage testing for SCLC. The first compound is picoplatin from Poniard Pharmaceuticals. Picoplatin is a platinum agent that is currently in a Phase III study in SCLC. The Phase III study looks to compare picoplatin in combination with best supportive care alone in patients who were refractory to platinum therapy or failed to respond to platinum therapy within six months. We will test INNO-206 in patients who initially had a response on platinum therapy.

The second compound in development in SCLC is amrubicin from Celgene. Amrubicin is a synthetic anthracycline currently approved in Japan for use in lung cancer. Celgene commenced a Phase III study in the second half of 2007 in relapsed and refractory SCLC patients based on Phase II data from Japan showing a survival of between 9.2 months and 11.7 months in this population.

Amrubicin and doxorubicin are both anthracyclines. We believe that the albumin-binding ability of INNO-206 will allow the compound to overcome many of the side effect issues typically associated with anthracyclines. We also believe that using albumin as a carrier will allow for higher dosing and greater efficacy.

There are currently two main competitors to INNO-406 in the Gleevec-resistant CML market, Dasatinib and nilotinib. Although both of these drugs are ahead of us in clinical testing and commercialization, we believe the head-start in development will not prove critical in the commercial setting, because CML is becoming a chronic condition much like HIV or depression and the market for treatment is large enough to accommodate several drugs.

Dasatinib from Bristol-Myers Squibb, was the first of the second-generation Bcr-Abl inhibitors to gain U.S. marketing approval from the FDA. Bristol-Myers Squibb began distributing the product in July 2006. Dasatinib has high potency in inhibiting Bcr-Abl and also inhibits Src, a family of kinases known to be involved in cell growth. In clinical studies, dasatinib has shown good activity in Gleevec-resistant patients. However, there have also been concomitant side effects, including serious and life threatening pleural effusion. In various studies presented to date, roughly 20% to 30% of the patients that start therapy are discontinuing. We believe a significant number of these patients are discontinuing due to the side effect profile of the drug. This side effect profile may be related to Src inhibition, but that has not yet been proven.

Nilotinib from Novartis AG, has completed its Phase II clinical study and was granted accelerated marketing approval by the FDA in October 2007 for the treatment of chronic phase and accelerated phase Philadelphia chromosome positive (Ph+) CML in adult patients resistant or intolerant to prior treatment with Gleevec. Nilotinib has potent activity against Bcr-Abl. In its Phase I clinical trial, Nilotinib showed good activity in Gleevec-resistant patients. In Phase II clinical data presented at the American Society for Hematology conference in 2006, nilotinib showed efficacy similar to dasatinib in Gleevec-resistant patients.

Other clinical compounds in development for CML include:

- Wyeth's SKI-606 is a dual Abl and Src kinase inhibitor similar to dasatinib and is currently in a Phase III trial in newly diagnosed Ph+ CML patients;
- Ceflatonin from Chemgenix, a plant alkaloid primarily targeting a single Bcr-Abl mutation known as T315I, which is in a Phase II/III clinical trial;
- Exelixis' XL228, a multi-kinase inhibitor that targets Src and Abl, has shown preclinical activity against the T315I mutation and is in a Phase I clinical trial in CML patients; and
- AP24534 from Ariad Pharmaceuticals is a multi-kinase inhibitor that targets Bcr-Abl including the T315I mutation and is in a Phase I clinical trial in CML patients.

We are aware of only one drug, rilutek, developed by Aventis Pharma AG, that has been approved by the FDA for the treatment of ALS. Many companies are working to develop pharmaceuticals to treat ALS, including Aeolus Pharmaceuticals, Mitsubishi Tanabe Pharma Corporation, Ono Pharmaceuticals, Trophos SA, Knopp

Neurosciences Inc., Faust Pharmaceuticals SA, Oxford BioMedica plc, Phytopharm plc and Teva Pharmaceutical Industries Ltd., as well as RXi. ALS patients often take over-the-counter supplements, including vitamin E, creatine and coenzyme Q10, or drugs such as lithium that are approved for other indications. ALS belongs to a family of neurodegenerative diseases that includes Alzheimer's, Parkinson's and Huntington's diseases. Due to similarities between these diseases, a new treatment for one such disease potentially could be useful for treating others. There are many companies producing and developing drugs used to treat neurodegenerative diseases other than ALS, including Amgen, Inc., Biogen Idec, Boehringer Ingelheim, Cephalon, Inc., Ceregene, Inc., Elan Pharmaceuticals, plc, Forest Laboratories, Inc., H. Lundbeck A/S, Phytopharm plc, UCB Group and Wyeth.

Current drug classes used to treat stroke include antiplatelet agents, anticoagulants, salicylates, neuroprotectants and thrombolytic agents. Prescription antiplatelet agents include Aggrenox by Boehringer Ingelheim, Plavix by Sanofi-Aventis and Bristol-Myers Squibb, and Ticlid by Roche Pharmaceuticals. Coumadin by Bristol-Myers Squibb and Jantoven by Upsher-Smith Laboratories are branded forms of warfarin, an anticoagulant. Moreover, Salicylates, like aspirin, are commonly used to treat patients after stroke. In Europe, Ferrer Grupo markets the neuroprotectant, Somazina. Activase, also known as tissue plasminogen activator, or t-PA, is a thrombolytic agent marketed by Genentech. Many new drug candidates are in development by pharmaceutical and biotech companies, including GlaxoSmithKline, Ipsen, Merck & Co., Ono Pharmaceuticals, PAION AG and Wyeth. In addition to drug therapy, companies such as Medtronic and Northstar Neurosciences are developing neurostimulation medical devices to aid in recovery after stroke.

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 biologic or 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 I trials consist of testing of the product candidate in a small number of patients or healthy volunteers, primarily for safety at one or more doses. Phase II trials, in addition to safety, evaluate the efficacy of the product candidate in a patient population somewhat larger than Phase I trials. Phase III 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 trials, 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. The FDA has granted fast track designation and orphan drug status to arimocloamol for the treatment of ALS.

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 Environmental Protection 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 July 1, 2009, we had 12 employees, two of whom were engaged in research and development activities and ten of whom were involved in management and administrative operations. Because we substantially completed the initial phase of the research and development activities performed at our San Diego facility and have determined to conduct our research and development activities through third parties for the foreseeable future, we have significantly reduced headcount and related expenses in the past three months.

Properties

Our headquarters are located in leased facilities in Los Angeles, California. The lease covers approximately 4,700 square feet of office space and expires in June 2012. This lease currently requires us to make monthly payments of approximately \$18,081.

We also lease approximately 10,000 square feet of office and laboratory space in San Diego, California. The lease expires in October 2010, although we have the option to extend the lease for up to two additional three-year terms. In May 2009, we substantially completed the initial phase of the research and development activities performed at the San Diego facility, and announced that we will conduct our research and development activities through third parties for the foreseeable future. As a result, we are exploring alternatives for the San Diego facility that might include subletting some or all of the premises. Our headquarters and laboratory facilities are sufficient for our current purposes.

We also acquired a sublease to approximately 5,526 square feet of office space at 555 Madison Avenue, New York, New York, in connection with our acquisition of Innovive in September 2008. This lease currently requires us to make annual payments of approximately \$210,000, plus certain taxes and operating expenses, and it expires on August 30, 2012. On December 4, 2008, we sub-leased the space to Red Pine Advisors LLC through August 29, 2012. Under the sub-sublease, we are entitled to base annual rent of approximately \$350,000, plus certain taxes and operating expenses.

RISK FACTORS

An investment in our shares involves a high degree of risk. Prior to making a decision about purchasing our shares, you should carefully consider the risks and uncertainties and all other information contained or incorporated by reference in this prospectus and in the prospectus supplement, including the risks and uncertainties discussed below, as well as any modification, replacement or update to these risks and uncertainties that are reflected in any subsequent filings we make with the SEC as described in the "Where You Can Find More Information" section of this prospectus. These risks and uncertainties are not the only ones facing us. Additional risks and uncertainties not presently known to us, or that we currently perceive as immaterial, may also harm our business. If any of these risks or uncertainties actually occurs, our business, results of operations and financial condition could be materially and adversely affected. In that case, the trading price of our common stock could decline, and you could lose all or part of your investment.

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 revenue. We incurred net losses of \$27.0 million, \$21.9 million and \$16.8 million for the years ended December 31, 2008, 2007 and 2006, respectively, and incurred net losses of \$4.0 million and \$6.1 million for the three months ended March 31, 2009 and 2008, respectively. We had an accumulated deficit as of March 31, 2009 of approximately \$196.1 million. We are likely to continue to incur losses unless and until we are able to commercialize one or more of our 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 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 our 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 revenues were \$6.3 million, \$7.5 million and \$2.1 million, respectively, for years ended December 31, 2008, 2007 and 2006, which included \$6.2 million, \$7.2 million and \$1.8 million, respectively, of deferred revenue recognized from our sale in August 2006 of a one-percent royalty interest in worldwide sales of arimoclomol for the treatment of ALS. Our revenues for the three months ended March 31, 2009 and 2008 were \$1.5 million and \$2.2 million, respectively, attributable to deferred revenue. We will have no significant recurring revenue unless we are able to commercialize one or more of our product candidates in development, which may require us to first enter into license or other strategic arrangements with third parties.

At March 31, 2009, we had cash, cash equivalents and short-term investments of \$21.9 million. We believe that our current resources will be sufficient to support our currently planned level of operations through into the third quarter of 2011. This estimate is based, in part, upon our currently projected expenditures for the remainder of 2009 and the first three months of 2010 of approximately \$10.7 million, which includes approximately \$0.7 million for our clinical program for tamibarotene, approximately \$0.3 million for our clinical program for INNO-206, approximately \$0.3 million for our clinical program for bafetinib, approximately \$0.7 million for our animal toxicology studies and related activities for arimoclomol, approximately \$1.0 million for operating our clinical programs, approximately \$1.1 million in connection with the outsourcing of research activities that previously had been conducted at our laboratory in San Diego, California, and approximately \$6.6 million for other general and administrative expenses. As described in the risk factor that follows below in this section, these projected expenditures are based upon numerous assumptions and subject to many uncertainties, and our actual expenditures may be significantly different from these projections.

If we obtain marketing approval as currently planned and successfully commercialize our product candidates, we anticipate it will take a minimum of three years, and possibly 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 has been materially and adversely affected by the downturn in the financial markets and poor economy, which have severely depressed the market for private investment in public equities, or PIPEs, transactions on which we have relied for raising needed capital. These conditions also have materially and adversely affected the market for our RXi shares. 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 announce and expect, or if our financial projections prove to be materially inaccurate, the commercialization of our products may be delayed and our business prospects may suffer.

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. For example, we have stated in our most recent Annual Report incorporated by reference in this prospectus supplement the expected timing of certain milestones relating to our tamibarotene, INNO-206 and arimoclomol clinical development programs.

We also may disclose projected expenditures or other forecasts for future periods such as the statements above in this prospectus supplement regarding our current projected expenditures for fiscal year 2009 and the first three months of 2010. 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 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 projections.

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.

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

All of our product candidates in development must be approved by the U.S. Food and Drug Administration, or 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:

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- difficulty in securing centers to conduct trials;
- difficulty in enrolling patients in conformity with required protocols or projected timelines;
 - unexpected adverse reactions by patients in trials;
 - difficulty in obtaining clinical supplies of the product;

- changes in or our inability to comply with FDA or foreign governmental product testing, manufacturing or marketing requirements;
- regulatory inspections of clinical trials or manufacturing facilities, which may, among other things, require us or our manufacturers or licensees to undertake corrective action or suspend or terminate the affected clinical trials if investigators find them not to be in compliance with applicable regulatory requirements;
- inability to generate statistically significant data confirming the safety and efficacy of the product being tested;
 - modification of the product during testing; and
 - reallocation of our limited financial and other resources to other clinical programs.

In addition, the FDA and other regulatory agencies may lack experience in evaluating our product candidates. For example, we are aware of only one drug that the FDA has approved to treat amyotrophic lateral sclerosis, commonly known as ALS, or Lou Gehrig's disease. This inexperience may lengthen the regulatory review process, increase our development costs and delay or prevent commercialization of arimoclomol or our other product candidates. 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 also 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 product candidates may fail to show that these product candidates are clinically safe and effective.

Our Phase IIa clinical trial and open-label extension clinical trial of arimoclomol for the treatment of ALS indicated that arimoclomol was safe and well-tolerated in patients, but the results of the open-label extension clinical trial indicated only a non-statistically significant trend of improvement in the revised ALS Functional Rating Scale, or ALSFRS-R, in the arimoclomol high-dose group as compared with reports of previous studies of untreated patients. This trial did not have a concurrent placebo control group, so we could draw no definitive conclusions with respect to efficacy. Further development of arimoclomol for ALS and stroke recovery, as well as clinical development of iroxanadine for diabetic foot ulcers, would require significant additional testing, and it is possible that the favorable safety data we observed in earlier trials may not be reproduced in any later trials.

Tamibarotene has been shown to be safe, well tolerated, and efficacious in the Japanese population. However, it is possible that the response to the drug may be different in American or European populations. Furthermore, the efficacy studies that led to approval in Japan occurred prior to the advent of the use of arsenic trioxide, or ATO, for second line therapy. It is possible that the current use of ATO could alter the safety or efficacy of tamibarotene. Finally, the FDA may not accept the Japanese studies as a database for safety in the US.

INNO-206 was no more toxic than free doxorubicin in a Phase I clinical trial and showed limited biological responses against tumors. However, these conclusions may not be reproducible in larger clinical trials. Furthermore, future clinical trials will likely include multiple dosing with INNO-206 instead of the single doses used in the Phase I clinical trial.

Later trials also may not yield statistically significant data indicating that these product candidates are 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 tamibarotene, INNO-206, arimocloamol or iroxanadine for these indications.

The FDA placed a clinical hold on our Phase IIb efficacy trial of arimocloamol for ALS, which will delay further development of arimocloamol.

In January 2008, the FDA placed a clinical hold on our Phase IIb clinical efficacy trial of arimocloamol for the treatment of ALS due to concerns relating to previous toxicology studies of arimocloamol in rats. We have completed additional animal toxicology studies to obtain additional safety data that we submitted to the FDA in the second quarter of 2009. Although we expect to the FDA to respond to that submission in the third quarter of 2009, we cannot be certain how long the FDA may take to complete its review. Depending on the outcome of the FDA's review, the FDA could require:

- additional toxicology or human studies prior to or in parallel with the resumption of clinical trials, which would result in substantial additional expenses and possible significant delays in completing the clinical trials; or
- changes in the design of our previously planned Phase IIb clinical efficacy trial, including a reduction in the planned dosage of arimocloamol, which could delay further or increase the cost of the trial, adversely affect our ability to demonstrate the efficacy of arimocloamol in the trial or cause the cancellation of the trial altogether due to one or more of these consideration.

If we are unable to resolve the FDA's safety concerns, the FDA may prohibit the resumption of trials of arimocloamol for the treatment of ALS and all other indications.

Even if we obtain regulatory approval for our product candidates, these product candidates may not achieve market acceptance or be profitable.

We do not expect to receive regulatory approvals for the commercial sale of any of our product candidates for several years, if at all. Even if we do receive regulatory approvals, the future commercial success of these drug candidates will depend, among other things, on their acceptance by physicians, patients, healthcare payors and other members of the medical community as therapeutic and cost-effective alternatives to commercially available products. If our product candidates fail to gain market acceptance, we may not be able to earn sufficient revenues to continue our business.

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

We currently plan to continue the development of tamibarotene for the treatment of APL through a third-party clinical trials management service, and may retain the services of site management and clinical research organizations to help conduct our other clinical trials. We may seek to complete the development of tamibarotene and market it ourselves if it is approved by the FDA. However, the completion of the development of tamibarotene and our other product candidates, as well as the marketing of these products, may require us to enter into strategic alliances, license agreements or other collaborative arrangements with other pharmaceutical companies under which those companies will be responsible for one or more aspects of the commercial development and eventual marketing of our products.

Our products 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 believe that obtaining and maintaining patent and other intellectual property rights for our technologies and potential products is critical to establishing and maintaining the value of our assets and our business. 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 own or have rights to patents and patent applications directed to INNO-206, bafetinib and our molecular chaperone amplification technologies, 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 U.S. 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 can take many years to issue, there may be currently pending applications, unknown to us, that may later result in issued patents that our arimoclomol, iroxanadine or other product candidates would infringe. In addition, if third parties file patent applications or obtain patents claiming technology also claimed by us in issued patents or pending applications, we may have to participate in interference proceedings in the US Patent and Trademark Office to determine priority of invention. If third parties file oppositions in foreign countries, we may also have to participate in opposition proceedings in foreign tribunals to defend the patentability of our foreign patent applications.

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

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

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

We have reported, in the past, material weaknesses in the effectiveness of our internal controls over financial reporting, and if we cannot maintain effective internal controls or provide reliable financial and other information, investors may lose confidence in our SEC reports.

Within the past several years:

- we identified a material weakness related to our accounting for an equity transaction by RXi and our tax withholding in connection with exercises of employee stock options. As a result, we restated our financial statements for the quarter ended June 30, 2007 and extended the filing of our quarterly report for the quarter ended September 30, 2007;

- we identified a material weakness related to our accounting for transactions at our former laboratory facility in Worcester, Massachusetts. As a result, we restated our financial statements for the quarters ended March 31, 2006, June 30, 2006 and September 30, 2006;
 - we improperly applied generally accepted accounting principles related to our accounting for deemed dividends incurred in connection with anti-dilution adjustments made to our outstanding warrants. This misapplication of accounting principles constituted a material weakness and caused us to twice restate our financial statements for the quarters ended March 31, 2005, June 30, 2005 and September 30, 2005 and for the year ended December 31, 2005, as well as restate our financial statements for the quarters ended March 31, 2006, June 30, 2006 and September 30, 2006; and
- we miscalculated pro forma employee stock option compensation figures disclosed in the footnotes to our financial statements. As a result, we restated our financial statements for the quarters ended March 31, 2005, June 30, 2005 and September 30, 2005 and for the year ended December 31, 2005.

In addition, we concluded in our annual report for the year ended December 31, 2007 and in our quarterly reports for the quarters ended March 31, 2008 and June 30, 2008, that our disclosure controls and procedures were ineffective as of those dates. Disclosure controls generally include controls and procedures designed to ensure that information required to be disclosed by us in the reports we file with the SEC is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms. In January 2008, we also filed an amendment to an SEC report to correct certain form errors.

Effective internal controls over financial reporting and disclosure controls and procedures are necessary for us to provide reliable financial and other reports and effectively prevent fraud. If we cannot maintain effective internal controls or provide reliable financial or SEC reports or prevent fraud, investors may lose confidence in our SEC reports, our operating results and the trading price of our common stock could suffer and we may become subject to litigation.

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. The pharmaceutical, biopharmaceutical and biotechnology industries are characterized by intense competition and rapid and significant technological advancements. Many companies, research institutions and universities are working in a number of areas similar to our primary fields of interest to develop new products. There also is intense competition among companies seeking to acquire products that already are being marketed. Many of the companies with which we compete have or are likely to have substantially greater research and product development capabilities and financial, technical, scientific, manufacturing, marketing, distribution and other resources than us and at least some of our present or future strategic partners or licensees.

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;

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- 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.

Companies that currently sell generic and proprietary compounds for the treatment of cancer and related diseases include, but are not limited to, Abraxis BioScience, Amgen, Sanofi-Aventis, Bayer, Bristol-Myers Squibb, Celgene, Cephalon, Genentech, Eli Lilly, Johnson & Johnson and Novartis. Alternative technologies are being developed to treat cancer and related diseases by numerous companies including Bristol-Myers Squibb, Eisai, Merck and Genentech, several of which are in advanced clinical trials. There also are FDA approved cancer therapies that are in the late stage of development by larger established companies for new cancer indications: Alimta (Eli Lilly), Avastin (Genentech), Eloxatin (Sanofi-Aventis), Erbitux (Bristol-Myers Squibb and Imclone Systems) and Tarceva (Genentech). Poniard Pharmaceuticals and Celgene are developing compounds for SCLC. Novartis and Bristol-Myers Squibb have each developed a treatment for chronic myelogenous leukemia that would compete with bafetinib. ATRA and Cephalon's Trisenox (arsenic trioxide) could compete with tamibarotene. In addition, companies pursuing different but related fields represent substantial competition. Any of these competing therapies could prove to be more effective than tamibarotene, INNO-206, bafetinib or any future therapy of ours.

We are aware of only one drug, Rilutek, which was developed by Aventis Pharma AG, that has been approved by the FDA for the treatment of ALS. Many companies are working to develop pharmaceuticals to treat ALS, including Aeolus Pharmaceuticals, Celgene Corporation, Mitsubishi Tanabe Pharma Corporation, Ono Pharmaceuticals, Trophos SA, Knopp Neurosciences Inc., Faust Pharmaceuticals SA, Oxford BioMedica plc, Phytopharm plc and Teva Pharmaceutical Industries Ltd., as well as RXi. ALS patients often take over-the-counter supplements, including vitamin E, creatine and coenzyme Q10, or drugs such as lithium that are approved for other indications. ALS belongs to a family of neurodegenerative diseases that includes Alzheimer's, Parkinson and Huntington's diseases. Due to similarities between these diseases, a new treatment for one such disease potentially could be useful for treating others. There are many companies producing and developing drugs used to treat neurodegenerative diseases other than ALS, including Amgen, Inc., Biogen Idec, Boehringer Ingelheim, Cephalon, Inc., Ceregene, Inc., Elan Pharmaceuticals, plc, Forest Laboratories, Inc., H. Lundbeck A/S, Phytopharm plc, UCB Group and Wyeth.

Current drug classes used to treat stroke include antiplatelet agents, anticoagulants, salicylates, neuroprotectants and thrombolytic agents. Prescription antiplatelet agents include Aggrenox by Boehringer Ingelheim, Plavix by Sanofi-Aventis and Bristol-Myers Squibb, and Ticlid by Roche Pharmaceuticals. Coumadin by Bristol-Myers Squibb and Jantoven by Upsher-Smith Laboratories are branded forms of warfarin, an anticoagulant. Moreover, Salicylates, like aspirin, are commonly used to treat patients after stroke. In Europe, Ferrer Grupo markets the neuroprotectant, Somazina. Activase, also known as tissue plasminogen activator, or t-PA, is a thrombolytic agent marketed by Genentech. Many new drug candidates are in development by pharmaceutical and biotech companies, including GlaxoSmithKline, Ipsen, Merck & Co., Ono Pharmaceuticals, PAION AG and Wyeth. In addition to drug therapy, companies such as Medtronic and Northstar Neurosciences are developing neurostimulation medical devices to aid in recovery after stroke.

Most of our competitors have substantially greater research and product development capabilities and financial, technical, scientific, manufacturing, marketing, distribution and other resources than us.

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

The agreement under which we have North American rights to tamibarotene provides for our payment of royalties based on net sales of any products, as well as aggregate payments of \$4.165 million upon meeting specified clinical, regulatory and sales milestones up to and including the first commercial sale of tamibarotene for the treatment of APL.

The agreement relating to our worldwide rights to INNO-206 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.

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.

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 U.S. 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).

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.

Our agreement by which we acquired rights to arimoclomol and our other molecular chaperone amplification product candidates provides for milestone payments by us upon the occurrence of specified regulatory filings and approvals related to the acquired products. In the event that we successfully develop arimoclomol or any of these other product candidates, these milestone payments could aggregate as much as \$3.7 million, with the most significant payments due upon the first commercialization of any of these products. In addition, our agreement with the ALS CRT requires us to pay a one-percent royalty interest on worldwide sales of arimoclomol for the treatment of ALS. Also, any future license, collaborative or other agreements we may enter into in connection with our development and commercialization activities may require us to pay significant milestone, license and other payments in the future.

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

We do not have the facilities or expertise to manufacture supplies of any of our product candidates, including tamibarotene, INNO-206, arimoclomol or iroxanadine. 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 tamibarotene and arimoclomol. However, we have no supply arrangements for the commercial manufacture of these product candidates 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 our 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 our products cannot be manufactured at an acceptable cost, the commercial success of our products may be adversely affected.

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 the 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 Phase II clinical trial of tamibarotene for APL, 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, or our ownership interest in RXi, 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.

Following our acquisition of Innovive in September 2008, we refocused our product development efforts on tamiboratene, which we acquired from Innovive and which we believe has the greatest near-term revenue potential of all of our other product candidates. 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, or to use shares of RXi common stock owned by us, or both, 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, or our ownership interest in RXi, or both, will be diluted accordingly.

We use hazardous materials and must comply with environmental, health and safety laws and regulations, which can be expensive and restrict how we do business.

Our research and development and manufacturing processes involve the controlled storage, use and disposal of hazardous materials, including biological hazardous materials. We are subject to federal, state and local regulations governing the use, manufacture, storage, handling and disposal of these materials and waste products. Although we believe that our safety procedures for handling and disposing of these hazardous materials comply with the standards prescribed by law and regulation, we cannot completely eliminate the risk of accidental contamination or injury from hazardous materials. In the event of an accident, we could be held liable for any damages that result. We could incur significant costs to comply with current or future environmental laws and regulations.

Risks Associated With Our Investment in RXi

We may sell or dispose of some of our RXi shares, and may not be able to do so on attractive terms.

As of July 1, 2009, we owned approximately 6,268,881 shares of common stock of RXi, or approximately 45% of the outstanding RXi common stock. RXi shares are listed on the Nasdaq Capital Market under the symbol "RXi." During the 12-month period ended June 30, 2009, the market prices for RXi shares as reported on the Nasdaq Capital Market has fluctuated from a high of \$12.25 per share to a low of \$2.71 per share, and the market price of RXi shares and the value of our RXi shares may continue to experience significant volatility. We believe that the downturn in the financial markets, in particular, and poor economy, generally, have contributed to the volatility of the market price of RXi shares.

We may determine to sell or otherwise dispose of our RXi shares in one or more transactions in order to obtain funds to carry on our operations or in connection with our acquisition of new technologies or products. There is no assurance, however, whether, or on what terms, we might be able to sell or dispose of our RXi shares. We believe that the downturn in the financial markets has adversely affected the market for shares of development-stage companies such as RXi.

If we undertake to sell our RXi shares, we may be unable to do so at attractive prices, if at all. In addition, any sales or other disposition of RXi shares by us, or the possibility of such sales or disposition, could adversely affect the market price of our remaining RXi shares.

If RXi undertakes future financings, our ownership interest in RXi may be diluted.

Under our agreement with RXi, with some exceptions, we will have preemptive rights to acquire a portion of any new securities sold or issued by RXi so as to maintain our percentage ownership of RXi. Depending upon the terms and provisions of any proposed sale of new securities by RXi, our financial condition and other factors, we may be unwilling or unable to exercise our preemptive rights. We agreed to waive our preemptive rights in connection with a private placement by RXi in June 2008, which resulted in a reduction in our percentage ownership of RXi from approximately 49% to approximately 45%. If RXi undertakes future issuances of equity securities, our percentage ownership interest in RXi may be diluted further.

We do not control RXi, and the officers, directors and other RXi stockholders may have interests that are different from ours.

Although we currently own a significant portion of RXi's outstanding common stock, we do not control its management or operations. RXi has its own board of directors and management, who are responsible for the affairs and policies of RXi and its development plans. We have entered into letter agreements with RXi and certain of its stockholders under which we agree to vote our shares of RXi common stock for the election of directors of RXi and to take other actions to ensure that a majority of RXi's board of directors are independent of us. The board of directors and other stockholders of RXi may have interests that are different from ours, and RXi may engage in actions in connection with its business and operations that we believe are not in our best interests.

Risks Associated With Our Common Stock

Our common stock may be delisted from the Nasdaq Capital Market if our stock price does not increase.

We received notice from the Nasdaq Stock Market on May 28, 2008 that we were not in compliance with the minimum \$1.00 closing bid price required by Nasdaq Marketplace Rule 4310(c)(4) and, in accordance with Marketplace Rule 4310(c)(8)(D), could regain compliance if, by November 24, 2008, our common stock closes at or above \$1.00 for 10 consecutive business days and we otherwise meet the Nasdaq's continuing listing requirements. Nasdaq subsequently announced that it had temporarily suspended until July 19, 2009 the enforcement of its rules requiring a minimum \$1.00 closing bid price. As a result, we will have until August 2009 to regain compliance with this rule, assuming no further actions by Nasdaq in this regard. However, in its original notice to us on May 28, 2008, Nasdaq also informed us that, if we did not regain compliance by the stated deadline, we would be granted up to an additional 180 calendar days (i.e. until February 2010) to regain full compliance while continuing to trade during such time if we meet the Nasdaq's initial listing requirements other than the minimum bid price rule. If we eventually fail to comply with this condition for continued listing and our common stock is delisted from the Nasdaq Small Capital Market, there is no assurance that our common stock will be listed for trading or quoted elsewhere and an active trading market for our common stock may cease to exist, which would materially and adversely impact the market value of our common stock.

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

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

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

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

We are also 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 you.

Our outstanding options and warrants and the availability for resale of our shares issued in our private financings may adversely affect the trading price of our common stock.

As of July 1, 2009, there were outstanding stock options and warrants to purchase approximately 18.5 million shares of our common stock at a weighted-average exercise price of \$1.24 per share. Our outstanding options and warrants could adversely affect our ability to obtain future financing or engage in certain mergers or other transactions, since the holders of options and warrants can be expected to exercise them at a time when we may be able to obtain additional capital through a new offering of securities on terms more favorable to us than the terms of outstanding options and warrants. For the life of the options and warrants, the holders have the opportunity to profit from a rise in the market price of our common stock without assuming the risk of ownership. The issuance of shares upon the exercise of outstanding options and warrants will also dilute the ownership interests of our existing stockholders. Many of our outstanding warrants contain anti-dilution provisions pertaining to dividends with respect to our common stock. Outstanding warrants to purchase approximately 9.3 million shares contain anti-dilution provisions that are triggered upon any issuance of securities by us below the prevailing market price of our common stock. Our distribution to our stockholders of RXi shares on March 11, 2008 required us to reduce the exercise price of those warrants. In the event that these anti-dilution provisions are triggered by us in the future, we would likewise be required to reduce the exercise price, and increase the number of shares underlying, those warrants, which would have a dilutive effect on our stockholders.

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

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

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

We 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 \$0.23 to \$5.49 per share since January 1, 2007, and it may continue to experience significant volatility from time to time. Our ability to raise capital has been materially and adversely affected by the downturn in the financial markets and poor economy, which have severely depressed the market for PIPEs transactions on which we have relied for raising needed capital.

Other factors that may affect the market price of our common stock include the following:

- announcements of regulatory developments or technological innovations by us or our competitors;
- changes in our relationship with our licensors and other strategic partners;
 - changes in our ownership of or other relationships with RXi;
 - 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.

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

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

USE OF PROCEEDS

Unless we indicate otherwise in the prospectus supplement, we expect to use the net proceeds we receive from the sale of our securities to augment our working capital and for general corporate purposes, including, but not limited to, product development activities, capital expenditures, potential acquisitions and other business opportunities. We may set forth in the prospectus supplement additional information on our intended use for the net proceeds received from the sale of any securities sold pursuant to that prospectus supplement.

THE SECURITIES THAT WE MAY OFFER

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

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

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

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

DESCRIPTION OF CAPITAL STOCK

Our authorized capital stock currently consists of 175,000,000 shares of common stock, \$.001 par value per share, and 5,000,000 shares of preferred stock, \$.01 par value per share.

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 supplement 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 non-assessable.

Preferred Stock

We are currently authorized to issue 5,000,000 shares of preferred stock, of which 15,000 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;

- 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 non-assessable 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 by-laws contain the following provisions that may have the effect of discouraging unsolicited acquisition proposals:

- our by-laws classify the board of directors into three classes with staggered three-year terms;
- under our by-laws, our board of directors may enlarge the size of the board and fill the vacancies;
- our 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 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.

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.

The applicable 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 debt securities and of the warrants that we may offer. If we elect to offer units, we will describe the specific terms of the units in a supplement to this prospectus. Among other things, the prospectus supplement will describe, to the extent applicable:

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

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 re-allowed or paid to dealers.

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

- at a fixed price or prices, which may be changed;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
 - at negotiated prices.

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

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

To facilitate the offering of securities, certain persons participating in the offering may engage in transactions that stabilize, maintain, or otherwise affect the price of the securities. This may include over-allotments or short sales of the securities, which involve the sale by persons participating in the offering of more securities than we sold to them. In these circumstances, these persons would cover such over-allotments or short positions by making purchases in the open market or by exercising their over-allotment option, if any. In addition, these persons may stabilize or maintain the price of the securities by bidding for or purchasing securities in the open market or by imposing penalty bids, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if securities sold by them are 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 are subject to the informational requirements of the Securities Exchange Act of 1934, or the Exchange Act, and are required to file annual, quarterly and other reports, proxy statements and other information with the SEC. You may inspect and copy these reports, proxy statements and other information at the public reference facilities maintained by the SEC in Washington, D.C. (100 F Street NE, Room 1580, Washington, D.C. 20549). Copies of such materials can be obtained from the SEC's public reference section at prescribed rates. You may obtain information on the operation of the public reference rooms by calling the SEC at (800) SEC-0330 or on the SEC website located at <http://www.sec.gov>.

Our common stock is traded on the Nasdaq Capital Market under the symbol "CYTR." Reports, proxy and information statements and other information concerning us also may be inspected at the offices of the National Association of Securities Dealers, Inc. located at 1735 K Street, N.W., Washington, D.C. 20006.

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

INCORPORATION OF INFORMATION FILED WITH THE SEC

The SEC allows us to incorporate in this prospectus "by reference" information contained in documents that we file with the SEC, which means that we can disclose important information to you by referring you to those other documents. The information incorporated by reference is an important part of this prospectus, and documents that we file with the SEC after the date of this prospectus will automatically update and, where applicable, modify or supersede any information set forth or incorporated by reference in this prospectus.

We incorporate by reference in this prospectus the documents listed below:

- our Annual Report on Form 10-K for the year ended December 31, 2008;

- our Quarter Report on Form 10-Q for the quarter ended March 31, 2009 filed on May 11, 2009
- our Current Reports on Form 8-K filed on May 5, 2009, May 12, 2009 and July 8, 2009, respectively (excluding any information furnished in such reports under Item 2.02, Item 7.01 or Item 9.01);
- 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;
 - our definitive Proxy Statement on Schedule 14A filed on May 11, 2009;
-
- 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; and
- any document that we file with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus and before the termination of this offering (other than any portion of such documents that are not deemed “filed” under the Exchange Act in accordance with the Exchange Act and applicable SEC rules). Information in these subsequent SEC filings will be deemed to be incorporated by reference as of the date we make the filing.

You may obtain a copy of the foregoing documents from us at no cost 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. As of July 1, 2009, TroyGould PC owned 70,000 shares of our common stock and warrants to purchase 7,146 shares of our common stock, as well as 23,491 shares of common stock of RXi.

EXPERTS

The consolidated financial statements, schedule and management's report on the effectiveness of internal control over financial reporting incorporated by reference in the Prospectus constituting a part of this Registration Statement have been audited by BDO Seidman, LLP, an independent registered public accounting firm, to the extent and for the periods set forth in their reports incorporated herein by reference, and are incorporated herein in reliance upon such reports given upon the authority of said firm as experts in auditing and accounting.