CYTRX CORP
Form POS AM
July 10, 2009

As filed with the Securities and Exchange Commission on July 10, 2009

Reg. No. 333-147605

SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Post-Effective Amendment No. 2
to
FORM S-3

REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

CYTRX CORPORATION
(Exact name of registrant as specified in its charter)

Delaware	58-1642750
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

CytRx Corporation
11726 San Vicente Boulevard, Suite 650
Los Angeles, California 90049
(Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)

Steven A. Kriegsman
CytRx Corporation
11726 San Vicente Boulevard., Suite 650
Los Angeles, California 90049
(310) 826-5648
(Name, address, including zip code, and telephone number, including area code, of agent for service)

With a copy to:

Benjamin S. Levin, Esq.	Sanford J. Hillsberg, Esq.
CytRx Corporation	Dale E. Short, Esq.
11726 San Vicente Boulevard, Suite 650	Troy & Gould Professional Corporation

Los Angeles, California 90049
Fax: (310) 826-6139

1801 Century Park East, Suite 1600, Los Angeles, California 90067
Fax: (310) 201-4746

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

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

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

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

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

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

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

CALCULATION OF REGISTRATION FEE

Title of each class of securities to be registered	Proposed maximum aggregate offering price(1)	Amount of registration fee
Common Stock, par value $.001 per share(2)		
Preferred Stock, $.01 par value per share		
Warrants		
Units		
Total(3)	$100,000,000(4)	$3,070(5)

(1) The securities registered by this registration statement may be sold separately, together with other securities registered hereunder or as units consisting of a combination of such securities. Pursuant to Rule 457(o) under the Securities Act of 1933 and General Instruction II.D to Form S-3 under the Securities Act of 1933, the number of shares, warrants or units of each class of securities registered hereunder is not specified. There is being registered

hereunder an indeterminate amount of common stock, preferred stock, warrants and units of the registrant as may from time to time be issued at indeterminate prices. The maximum offering price per class of securities will be determined from time to time by the registrant in connection with the issuance of the securities registered by this registration statement. However, in no event will the maximum aggregate offering price of all securities issued under this registration statement exceed $100,000,000 or such lesser aggregate amount permitted under General Instruction I.B.6 to Form S-3 under the Securities Act of 1933.

(2) Each share of common stock will be accompanied by one Series A Junior Participating Preferred Stock Purchase Right that trades with the common stock. The value, if any, attributable to this right is reflected in the market price of common stock. Prior to the occurrence of certain events, none of which has occurred as of the date of this registration statement, the rights will not be exercisable or evidenced separately from the common stock.

(3) Pursuant to Rule 416 under the Securities Act of 1933, this registration statement also registers such indeterminate amounts of securities as may be issued upon conversion of, or in exchange for, the securities registered hereunder and such indeterminate number of shares of common stock and preferred stock as may be issued from time to time upon conversion or exchange as a result of stock splits, stock dividends or similar transactions.

(4) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(o) under the Securities Act of 1933.

(5) Previously paid.

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

The information in this prospectus is not complete and may be changed. These shares may not be sold until the registration statement filed with the Securities and Exchange Commission becomes effective. This prospectus is not an offer to sell these shares, and it is not a solicitation of an offer to buy these shares, in any state where the offer or sale is not permitted.

SUBJECT TO COMPLETION, JULY 10, 2009

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 10, 2009

TABLE OF CONTENTS

ABOUT THIS PROSPECTUS

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

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

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

You should rely only on the information provided in this prospectus and in the prospectus supplement, including any information incorporated by reference. For more details on information incorporated herein by reference, you should review the discussion contained under the heading "Incorporation of 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," "anticip 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 anthracyline-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, Dasatanib 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, salycylates, 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 neroprotectant, 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 arimoclomol 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-subleased 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:

- 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 arimoclomal 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, arimoclomol or iroxanadine for these indications.

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

In January 2008, the FDA placed a clinical hold on our Phase IIb clinical efficacy trial of arimoclomol for the treatment of ALS due to concerns relating to previous toxicology studies of arimoclomol 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 arimoclomol, which could delay further or increase the cost of the trial, adversely affect our ability to demonstrate the efficacy of arimoclomol 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 arimoclomol 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, an