

CYTRX CORP  
Form S-3  
April 13, 2006

**Table of Contents**

As filed with the Securities and Exchange Commission on April 13, 2006

Reg. No. \_\_\_\_\_

**SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549**

**FORM S-3  
REGISTRATION STATEMENT  
UNDER  
THE SECURITIES ACT OF 1933**

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

**Delaware**  
(State or other jurisdiction of  
incorporation or organization)

**58-1642750**  
(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:**  
**Sanford J. Hillsberg, Esq.**  
**Dale E. Short, Esq.**  
**Troy & Gould Professional Corporation**  
**1801 Century Park East, Suite 1600, Los Angeles, California 90067**  
**(310) 553-4441**

**Approximate date of commencement of proposed sale to public:** As soon as practicable after this Registration Statement becomes effective.

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.

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. o

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. o

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. o

**CALCULATION OF REGISTRATION FEE**

<b>Title of each class of securities to be registered</b>	<b>Amount to be registered(1)</b>	<b>Proposed maximum offering price per share</b>	<b>Proposed maximum aggregate offering price</b>	<b>Amount of registration fee</b>
Common Stock, par value \$ .001 per share	11,050,796	\$2.20(2)	\$24,311,749(2)	\$2,601.36
Common Stock, par value \$ .001 per share	6,070,954(3)	\$1.54(4)	\$9,349,269(4)	\$1,000.38
Total Registration Fee				\$3,601.74

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

- (2) Estimated solely for the purpose of calculating the registration fee. Based, pursuant to Rule 457(c), on the average of the high and low sale prices of common stock as reported on Nasdaq SmallCap Market on April 11, 2006.
  
- (3) Represents shares issuable upon exercise of outstanding warrants. In accordance with Rule 416, there is also being registered hereunder such indeterminate number of additional shares of common stock as may become issuable upon exercise of the warrants to prevent dilution resulting from stock splits, stock dividends or similar transactions.
  
- (4) Estimated solely for the purpose of calculating the registration fee. Based, pursuant to Rule 457(g), on the exercise

price of  
warrants.

**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.**

---

Table of Contents

**SUBJECT TO COMPLETION, APRIL 13, 2006**  
**PROSPECTUS**  
**CYTRX CORPORATION**  
**17,121,750 Shares**  
Common Stock

This prospectus relates to shares of our common stock offered for resale by the selling securityholders listed in this prospectus under Selling Securityholders. Each of the shares is accompanied by one Series A Junior Participating Preferred Stock Purchase Right that trades with our common stock. Of the shares offered, 11,050,796 shares are currently outstanding and 6,070,954 shares are issuable upon the exercise of outstanding warrants to purchase our common stock. The number of shares being offered by the selling securityholders is subject to increase in certain events by reason of so-called antidilution provisions contained in the warrants. The selling securityholders holding warrants must first exercise the warrants and acquire the underlying shares from us before they can resell those shares under this prospectus.

We will receive the exercise price of the warrants described in this prospectus to the extent they are exercised for cash, but we will not otherwise receive any proceeds in connection with the sale of the shares by the selling securityholders. We will bear the costs and expenses of registering the shares offered by the selling securityholders. The selling securityholders will bear any commissions and discounts attributable to their sales of the shares.

Our common stock is traded on the Nasdaq Capital Market under the symbol CYTR. On April 11, 2006, the last sale price of our common stock as reported on the Nasdaq Capital Market was \$2.14.

The selling securityholders may offer the shares from time-to-time to or through brokers, dealers or other agents, or directly to other purchasers, in one or more market transactions or private transactions at prevailing market or at negotiated prices.

An investment in our common stock involves a high degree of risk. Before purchasing any shares, you should consider carefully the risks described under Risk Factors beginning on page 12.

**Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved the common stock or determined that this prospectus is complete or accurate. Any representation to the contrary is a criminal offense.**

The date of this prospectus is \_\_\_\_\_, 2006

You should rely only on the information contained or incorporated by reference in this prospectus and any supplement. We have not authorized any other person to provide you with different or additional information. If anyone provides you with different or additional information, you should not rely on it. This prospectus is not an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in or incorporated by reference in this prospectus and any supplement is accurate as of its date only. Our business, financial condition, results of operations, and prospects may have changed since that date.

**TABLE OF CONTENTS**

	<b>Page</b>
<u>Prospectus Summary</u>	1
<u>Forward-Looking Statements</u>	2
<u>The Company</u>	2
<u>Risk Factors</u>	12
<u>Use of Proceeds</u>	22
<u>Selling Securityholders</u>	23
<u>Plan of Distribution</u>	27
<u>Where You Can Find More Information</u>	28
<u>Incorporation of Information Filed with the SEC</u>	29
<u>Legal Matters</u>	29
<u>Experts</u>	29
<u>EX-5</u>	
<u>Exhibit 23.2</u>	

**Table of Contents**

**PROSPECTUS SUMMARY**

*This summary highlights information contained elsewhere in this prospectus. It does not contain all of the information you should consider before investing in our common stock. You should carefully read the entire prospectus, including the information under the heading Risk Factors, before making an investment decision.*

*Throughout this prospectus, the terms we, us, our, and our company refer to CytRx Corporation, a Delaware corporation, unless the context suggests otherwise.*

**Our Company**

CytRx Corporation is a biopharmaceutical research and development company, based in Los Angeles, California, with an obesity and type 2 diabetes research laboratory in Worcester, Massachusetts. We are in the process of developing products, primarily in the areas of small molecule therapeutics and ribonucleic acid interference, or RNAi, for the human health care market. Our small molecule therapeutics efforts include clinical development of three oral drug candidates that we acquired in October 2004, including a Phase II trial initiated in September 2005 with our lead small molecule product candidate arimoclomol for the treatment of amyotrophic lateral sclerosis (ALS or Lou Gehrig's disease), as well as drug discovery operations conducted at our Massachusetts laboratory. In addition to our work in small molecule therapeutics and RNAi, we recently announced that a novel HIV DNA + protein vaccine exclusively licensed to us and developed by researchers at the University of Massachusetts Medical School, or UMMS, and Advanced BioScience Laboratories, and funded by the National Institutes of Health, demonstrated promising interim Phase I clinical trial results that indicate its potential to produce potent antibody responses with neutralizing activity against multiple HIV viral strains. We have also entered into strategic alliances with respect to the development of several other products using our other technologies.

**The Offering**

Common stock offered by the selling security holders	17,121,750 shares of our common stock, consisting of 11,050,796 currently outstanding shares and 6,070,954 shares issuable upon the exercise of outstanding warrants.
Common stock currently outstanding	70,457,988 shares as of March 31, 2006.
Common stock to be outstanding after the offering	76,528,942 shares, assuming the issuance of all 6,070,954 shares that are issuable upon exercise of the warrants described in this prospectus and without giving effect to any other issuances of common stock subsequent to March 31, 2006.
Risk factors	An investment in our common stock involves significant risks. See Risk Factors beginning on page 12.



**Table of Contents**

**FORWARD-LOOKING STATEMENTS**

In addition to the other information contained in this prospectus, investors should carefully consider the risk factors disclosed in this prospectus, including those beginning on page 12, in evaluating an investment in our common stock. This prospectus and the documents incorporated herein by reference include forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act. All statements other than statements of historical fact are forward-looking statements for purposes of these provisions, including any projections of financial items, any statements of the plans and objectives of management for future operations, any statements concerning proposed new products or services, any statements regarding future economic conditions or performance, and any statement of assumptions underlying any of the foregoing. In some cases, forward-looking statements can be identified by the use of terminology such as may, will, expects, plans, anticipates, estimates, potential, or could or the negative thereof or other comparable terminology. Although we believe that the expectations reflected in the forward-looking statements contained herein and in such incorporated documents are reasonable, there can be no assurance that such expectations or any of the forward-looking statements will prove to be correct, and actual results could differ materially from those projected or assumed in the forward-looking statements.

Our future financial condition and results of operations, as well as any forward-looking statements, are subject to inherent risks and uncertainties, including but not limited to the risk factors set forth under the heading Risk Factors in this prospectus, and including risks or uncertainties regarding the scope of the clinical testing that may be required by regulatory authorities for our molecular chaperone co-induction drug candidates, including with respect to arimoclomol for the treatment of amyotrophic lateral sclerosis (ALS or Lou Gehrig's disease), our HIV vaccine candidate and our other product candidates, and the outcomes of those tests; uncertainties related to the early stage of our diabetes, obesity, cytomegalovirus, or CMV, and ALS research; the need for future clinical testing of any small molecules and products based on ribonucleic acid interference, or RNAi, that may be developed by us; the significant time and expense that will be incurred in developing any of the potential commercial applications for our small molecules or RNAi technology; risks or uncertainties related to our ability to obtain capital to fund our ongoing working capital needs, including capital required to fund the RNAi development activities to be conducted by our planned new subsidiary; and risks relating to the enforceability of any patents covering our products and to the possible infringement of third party patents by those products.

All forward-looking statements and reasons why results may differ included in this prospectus are made as of the date hereof, and we assume no obligation to update any such forward-looking statement or reason why actual results might differ.

**THE COMPANY**

**General**

We are a biopharmaceutical research and development company, based in Los Angeles, California, with an obesity and type 2 diabetes research laboratory in Worcester, Massachusetts. We are in the process of developing products, primarily in the areas of small molecule therapeutics and ribonucleic acid interference, or RNAi, for the human health care market. Our small molecule therapeutics efforts include clinical development of three oral drug candidates that we acquired in October 2004, including a Phase II trial initiated in September 2005, as well as drug discovery operations conducted at our laboratory in Worcester, Massachusetts. RNAi is a relatively recent technology for silencing genes in living cells and organisms, and we are aware of only four clinical tests of therapeutic applications using RNAi that have been initiated by any party. In addition to our work in RNAi and small molecule therapeutics, we recently announced that a novel HIV DNA + protein vaccine exclusively licensed to us and developed by researchers at the University of Massachusetts Medical School, or UMMS, and Advanced BioScience Laboratories, and funded by the National Institutes of Health, demonstrated promising interim Phase I clinical trial results that indicate its potential to produce potent antibody responses with neutralizing activity against multiple HIV viral strains. We have also entered into strategic alliances with respect to the development of several other products using our other technologies.

On October 4, 2004, we acquired all of the clinical and pharmaceutical and related intellectual property assets of Biorex Research & Development, RT, or Biorex, a Hungary-based company focused on the development of novel small molecules based on molecular chaperone co-induction technology, with broad therapeutic applications in



**Table of Contents**

neurology, type 2 diabetes, cardiology and diabetic complications. The acquired assets include three oral, clinical stage drug candidates and a library of 500 small molecule drug candidates. We recently entered the clinical stage of drug development with the initiation of a Phase II clinical program with our lead small molecule product candidate arimoclomol for the treatment of amyotrophic lateral sclerosis (ALS or Lou Gehrig's disease). Arimoclomol has received Orphan Drug and Fast Track designation from the U.S. Food and Drug Administration.

The initial Phase II clinical trial that we have initiated for arimoclomol for ALS (which we refer to as the Phase IIa trial) is a multicenter, double-blind, placebo-controlled study of approximately 80 ALS patients enrolled at ten clinical centers across the U.S. Patients will receive either placebo (a capsule without drug), or one of three dose levels of arimoclomol capsules three times daily, for a period of 12 weeks. This treatment phase will be immediately followed by a one-month period without drug. The primary endpoints of this Phase IIa trial are safety and tolerability. Secondary endpoints include a preliminary evaluation of efficacy using two widely accepted surrogate markers, the revised ALS Functional Rating Scale (ALSFRS-R), which is used to determine patients' capacity and independence in 13 functional activities, and Vital Capacity (VC), an assessment of lung capacity. The trial is powered to monitor only extreme responses in these two categories. We recently announced initiation of an open-label (*i.e.*, the medication is no longer blinded to the patients or their doctor) extension of this clinical trial. Patients who complete the Phase IIa study and who still meet the eligibility criteria may have the opportunity to take arimoclomol, at the highest investigative dose, for as long as an additional 6 months.

Depending upon the results of the Phase IIa trial, we plan to initiate a subsequent Phase II trial (which we refer to as the Phase IIb trial) that will be powered to detect more subtle efficacy responses. Although this second trial is still in the planning stages and will be subject to FDA approval, it is expected to include approximately 300 ALS patients recruited from 25 clinical sites and will take approximately 18 months after initiation to complete.

The acquisition of the molecular chaperone co-induction technology from Biorex represented a continuation of our business strategy, adopted subsequent to our merger with Global Genomics, in July 2002, to conduct further research and development efforts for our pre-merger adjuvant and co-polymer technologies, including Flocor and Tranzfect, through strategic relationships with other pharmaceutical companies, and to focus our efforts on acquiring and developing new technologies and products to serve as the foundation for the future of the company.

In April 2003, we acquired our first new technologies by entering into exclusive license agreements with UMMS covering potential applications for its proprietary RNAi technology in the treatment of specified diseases and in the identification and screening of novel protein targets. In May 2003, we broadened our strategic alliance with UMMS by acquiring an exclusive license from it covering a proprietary DNA-based HIV vaccine technology. In July 2004, we further expanded our strategic alliance with UMMS by entering into a collaboration and invention disclosure agreement with UMMS under which UMMS will disclose to us certain new technologies developed at UMMS over a three-year period pertaining to RNAi, diabetes, obesity, neurodegenerative diseases (including ALS) and CMV, and will give us an option, upon making a specified payment, to negotiate an exclusive worldwide license to the disclosed technologies on commercially reasonable terms. Approximately one year remains on the technology disclosure option. As part of our strategic alliance with UMMS, we agreed to fund certain discovery and pre-clinical research at UMMS relating to the use of our technologies, licensed from UMMS, for the development of therapeutic products within certain fields.

In conjunction with some of our work with UMMS, we operate a research and development laboratory in Worcester, Massachusetts whose goal is to develop small molecule and RNAi-based therapeutics for the prevention, treatment and cure of obesity and type 2 diabetes. This laboratory is focusing on using our proprietary RNAi gene silencing technology, combined with genomic and proteomic based drug discovery technologies, to accelerate the process of screening and identifying potential proprietary drug targets and pathways for these diseases. Through this laboratory, we are seeking to develop orally active drugs against promising targets and pathways relevant to obesity and type 2 diabetes.

Although we intend to internally fund the early stage development work for certain product applications (including obesity, type 2 diabetes and ALS) and may seek to fund the completion of the development of certain of these product applications (such as arimoclomol for ALS), we may also seek to secure strategic alliances or license agreements with larger pharmaceutical or biotechnology companies to fund the early stage development work for other gene silencing

product applications and for subsequent development of those potential products where we fund the early stage development work.

**Table of Contents**

Prior to 2003, our primary technologies consisted of Flocor, an intravenous agent for treatment of sickle cell disease and other acute vaso-occlusive disorders, and TranzFect, a delivery technology for DNA and conventional-based vaccines. In October 2003, we entered into a strategic relationship with another entity to complete the development of Flocor. Our TranzFect technology has been licensed to two companies. We have granted a third party an option to license our TranzFect technology for development as a potential DNA-based prostate cancer adjuvant and may also seek to license this technology as a potential conventional adjuvant for hepatitis C, human papilloma virus, herpes simplex virus and other viral diseases. Adjuvants are agents added to a vaccine to increase its effectiveness. In addition, we may seek to license TranzFect for use as a non-clinical research reagent to increase transfection *in vitro* or in laboratory animals. Flocor and TranzFect are further described under Pre-Global Genomics Merger Technologies.

In addition, through our merger with Global Genomics, we acquired minority interests in two development-stage genomics companies, Blizzard and Psynomics. In 2003, we recorded a write-off of our investments in those companies. Our decision to record the write-off was based upon several factors. Those investments, and the write-off of those investments, are further described under Genomics Investments.

***Molecular Chaperone Co-Induction Platform***

The synthesis of proteins is a normal part of every cell's activity that is essential for life. Proteins are linear chains of building blocks known as amino acids. In order to function normally in a cell, proteins must fold into particular three dimensional shapes. During stressful conditions (*e.g.* during certain disease states), proteins can fold into inappropriate shapes that result in aggregation of proteins, which can be toxic to the cell. As an example, it is believed that mis-folding and aggregation of certain mutated forms of the superoxide dismutase 1 (SOD1) protein leads to the death of motor neurons that causes ALS.

In nature, the cell has developed molecular chaperone proteins to deal with these potentially toxic mis-folded proteins. Molecular chaperones are a key component of a universal cellular protection, maintenance and repair mechanism that helps ensure that newly synthesized proteins are complete, taken to the correct position within the cell's structure, and correctly folded. Molecular chaperones detect proteins that are mis-folded, and have the ability to refold those proteins into the appropriate, non-toxic shape. However, if the protein is so badly mis-folded that it cannot be repaired, the molecular chaperones also have the ability to tag the toxic protein for destruction by the cell. This tag, called ubiquitin, directs the mis-folded protein to a cellular apparatus called the proteasome, whose function is to degrade the protein into its constituent amino acids for recycling.

A core element of the cell's stress-management techniques is known as the heat shock response. Although this response was so-named because it was initially discovered by subjecting cells to heat stress, it is now known that the heat shock response is generally induced by a variety of physical and chemical stresses. As a cell comes under stress, proteins begin to mis-fold into toxic shapes. The heat shock response (also referred to as the stress response) increases the synthesis of molecular chaperones that then repair or degrade the mis-folded proteins.

The stress response can be an important mechanism for cellular survival during certain acute physical stresses. For instance, prior induction of the stress response can protect tissue culture cells from heat-induced cell death. However, it appears that the constant stress that occurs as a result of chronic disease dulls the stress response and erodes the effectiveness of the mechanism. For instance, although the stress response is slightly induced in the motor neurons of mice in an ALS model, the level of expression is apparently insufficient to repair the damage and the mice still die from the disease.

We believe that by boosting the stress response to higher levels, the progression of chronic diseases like ALS can be slowed, halted or reversed. In test tube experiments, mammalian cells engineered to have increased amounts of molecular chaperones are protected against a variety of otherwise lethal stresses. In animal studies, mice that have been genetically engineered to have increased amounts of a molecular chaperone had improved heart function after an experimental heart attack. Increased molecular chaperone amounts also significantly increased the lifespan of mice with a disease similar to ALS, called spinal and bulbar muscular atrophy. We believe that these studies give scientifically accepted support for new drugs like arimoclomol that are capable of boosting the stress response.

Among the assets acquired from Biorex were several drug candidates whose mechanism of action is believed to be the co-induction of the stress response, meaning that they do not seem to activate the stress response by



**Table of Contents**

themselves, but instead they amplify the production of molecular chaperone proteins that are already activated by disease-induced cellular stress. These drug candidates thus may selectively amplify molecular chaperone proteins specifically in diseased tissue, which would minimize potential drug side-effects. The amplification of this fundamental protective mechanism may have powerful therapeutic and prophylactic potential, with the potential for an extremely broad field of medical therapeutic utility.

We believe that our molecular chaperone co-induction drug candidates can potentially improve the cell's natural capability to resist the toxic effects of protein mis-folding, caused by both acute and chronic diseases. Thus, these orally available small molecule drug candidates may accomplish some of the same goals as RNAi, as described below, but accomplish them by repairing or degrading the offending proteins, instead of degrading their corresponding mRNAs. Since the specificity for the recognition of mis-folded proteins is an intrinsic feature of the amplified molecular chaperones, it is not necessary to identify the actual molecular target of the stress-induced damage. As a result, these drug candidates may allow broader therapeutic utility for the removal of damaged proteins compared to that of RNAi.

We are not aware of other pharmaceutical companies developing small molecule co-inducers of molecular chaperones. At present, a few potential drug candidates have been reported in scientific papers to activate molecular chaperone expression, but these do not require pre-activation of the stress response, and therefore these drug candidates may simply represent a stress to the cell.

***RNAi Platform Technology***

RNAi technology uses short double-stranded RNA, or dsRNA, molecules to silence targeted genes and, as a result, is commonly referred to as gene silencing. RNAi has been shown to effectively silence targeted genes within living cells with great specificity and potency. As a result, RNAi technology is able to effectively silence targeted genes without impacting other, non-targeted, genes.

RNA is a polymeric constituent of all living cells and many viruses, consisting of a long, usually single-stranded chain of alternating phosphate and ribose units with the bases adenine, guanine, cytosine, and uracil bonded to the ribose. The structure and base sequence of RNA are determinants of protein synthesis and the transmission of genetic information. RNAi is a technique of using short pieces of double-stranded RNA to precisely target the messenger RNA, or mRNA, of a specific gene. The end result is the destruction of the specific mRNA, thus silencing that gene.

RNAi is regarded as a significant advancement in gene silencing and was featured in *Science* magazine as the Breakthrough of the Year in 2002. Delivery of RNAi can be useful in laboratory cell culture experiments and in animals (including humans) to target specific mRNAs, thus reducing the levels of the corresponding specific protein product that is coded for by that RNA in the targeted cells. This allows the use of RNAi either as an effective drug discovery tool or potentially as a therapeutic product itself. We intend to develop RNAi technology as both a discovery tool to help identify classical, orally-available small molecule drugs and, potentially through the creation of a new subsidiary, for direct therapeutic applications when technically feasible. As a drug discovery tool, we use RNAi to identify and validate novel protein targets, which could then be used to discover small molecule therapeutics for the treatment and prevention of diseases such as obesity and type 2 diabetes. As a therapeutic, we are conducting pre-clinical RNAi efficacy studies to determine whether to proceed with human clinical trials using RNAi to silence specific genes that cause certain forms of ALS, CMV retinitis, and type 2 diabetes. In January 2004, Tariq Rana, a scientific authority in delivery and stability of RNAi, and in March 2004, Dr. Craig Mello, the co-discoverer of RNAi, each joined our Scientific Advisory Board and they act in an advisory capacity to help us develop RNAi therapeutics for specific diseases. We are currently pursuing a plan, subject to obtaining necessary funding, to transfer all of our RNAi therapeutics assets into a newly-formed subsidiary to accelerate the development and commercialization of drugs based on RNAi technology. In such event, the Company would continue to use its RNAi gene silencing technology as a drug discovery tool to facilitate its small molecule drug discovery program.

In mammals and human cells, gene silencing can be triggered by dsRNA molecules present in the cell's cytoplasm (the region inside the cell membrane but outside the cell nucleus). Specific enzymes (proteins) in the cell called dicer enzymes cut the dsRNA to form small interfering RNA, or siRNA. These siRNA are approximately 21 to 25 nucleotide long pieces of RNA. The siRNA then interact with other cellular proteins to form the RNA-induced





**Table of Contents**

silencing complex, or RISC, which causes the unwinding of the bound siRNA. This unwound strand of the siRNA can then act as a template to seek out and bind with the complementary target mRNA, which carries the coding, or instructions, from the cell nucleus DNA. These instructions determine which proteins the cell will produce. When the siRNA-loaded RISC binds with the corresponding mRNA, that message is degraded and the cell does not produce the specific protein that it encodes. Since the siRNA can be designed to specifically interact with a single gene through its mRNA, it can prevent the creation of a specific protein without affecting other genes.

One reason for the potential of RNAi to be effective, where previous nucleic acid-based technologies have, to date, been unsuccessful, is that the cell already has in place all of the enzymes and proteins to effectively silence genes once the dsRNA is introduced into the cell. This is in direct contrast to the older technology of antisense, where there were no known proteins present in the cells to facilitate the recognition and binding of the antisense molecule to its corresponding mRNA.

Another reason for the interest in RNAi is its potential to completely suppress or eliminate the viral replicon. A replicon is a DNA or RNA element that can act as a template to replicate itself. Once a virus is established in a cell, there are very few drugs that are effective in eliminating the virus. The RNAi process, however, has the potential of eliminating viral nucleic acids and, therefore, to cure certain viral diseases. Development work on RNAi is still at an early stage, and we are aware of only four clinical trials using RNAi, namely trials for age-related macular degeneration by Acuity Pharmaceuticals and Sirna Therapeutics, for respiratory syncytial virus by Alnylam Pharmaceuticals and for diabetic macular edema by Acuity Pharmaceuticals.

**Product Development****ALS**

The development of therapeutics for the treatment of various forms of ALS is an area of significant interest for us. ALS is a debilitating disease. According to the ALS Survival Guide, 50% of ALS patients die within 18 months of diagnosis and 80% of ALS patients die within five years of diagnosis. According to the ALS Association, in the United States, alone, approximately 30,000 people are living with ALS and nearly 6,000 new cases are diagnosed each year.

We recently entered the clinical stage of drug development in ALS with the initiation of a Phase II clinical program with our lead small molecule product candidate arimoclomol for the treatment of ALS. Arimoclomol has received Orphan Drug and Fast Track designation from the U.S. Food and Drug Administration. The initial portion of the Phase II clinical program was initiated in September 2005. Enrollment in this Phase IIa trial was completed in April 2006.

In October 2003, we entered into sponsored research agreements with UMMS and Massachusetts General Hospital, pursuant to which we sponsored certain ALS research at those institutions utilizing our proprietary RNAi gene silencing technology targeted at the mutant SOD1 gene, which is the subject of the ALS technology we have licensed from UMMS. The mutant SOD1 gene is responsible for causing ALS in a subset of the 10% of all ALS patients who suffer from the familial, or genetic, form of the disease.

Dr. Zuoshang Xu, an Associate Professor of Biochemistry and Molecular Pharmacology at UMMS, is the principal investigator under our sponsored research agreement with UMMS, through which we have agreed to fund approximately \$870,000 of research related to the development of an RNAi therapeutic targeting the mutant form of SOD1 that causes certain forms of ALS, of which \$655,000 had been paid as of December 31, 2005. We anticipate that the development of this program will be continued by our planned RNAi subsidiary.

Dr. Robert B. Brown, Jr., a Professor of Neurology at Harvard Medical School, Founder and Director of the Cecil B. Day Laboratory for Neuromuscular Research and a co-discoverer of the mutant SOD1 gene as a cause for certain ALS cases, is the principal investigator under our sponsored research agreement with Massachusetts General Hospital. Under the agreement, we have funded approximately \$556,000 of sponsored research at Massachusetts General Hospital to increase our basic understanding of certain aspects of the ALS disease process. In March 2004, Dr. Brown joined our Scientific Advisory Board and entered into a consulting agreement with us.

**Table of Contents*****University of Massachusetts Medical School***

Through our strategic alliance with UMMS, we have acquired the rights to a portfolio of technologies, including the rights to use UMMS' s proprietary RNAi technology in the identification and screening of novel protein targets and as a potential therapeutic in certain defined areas that include obesity, type 2 diabetes, ALS and CMV, as well as a DNA-based HIV vaccine technology. In addition, we have entered into a collaboration and invention disclosure agreement with the UMMS under which UMMS will disclose to us certain new technologies developed at UMMS over a three-year period pertaining to RNAi, diabetes, obesity, neurodegenerative diseases (including ALS) and CMV and will give us an option, upon making a specified payment, to negotiate an exclusive worldwide license to the disclosed technologies on commercially reasonable terms. Approximately one year remains on the technology disclosure option.

The HIV subunit vaccine technology that we have licensed from UMMS is based upon a unique mixture of pieces of human HIV-1 primary isolates from several genetic subtypes of HIV. These pieces, called HIV envelope proteins, are not sufficient for viral replication and therefore cannot lead to accidental infection by HIV. This polyvalent naked DNA (isolated, purified DNA) vaccine approach has the potential advantages of maintaining efficacy despite the high mutation rate of HIV, a broader immune response against divergent HIV-1 glycoproteins and the possible ability to neutralize a wide spectrum of HIV-1 viruses. UMMS has conducted animal studies of this vaccine, and UMMS and Advanced BioScience Laboratories, or ABL, which provides an adjuvant for use with the vaccine, received a \$16 million grant from the NIH. This grant funded a Phase I clinical trial of a vaccine candidate using our licensed technology. We have previously announced that the vaccine candidate demonstrated very promising interim Phase I clinical trial results that indicate its ability to produce potent antibody responses with neutralizing activity against multiple HIV viral strains, and we expect to announce final results from the Phase I clinical trial in mid-2006. We have a commercial relationship with ABL which gives us the ownership of, and responsibility for, the further development of the vaccine and subsequent FDA registration following the completion of the Phase I trial. We do not have a commercial relationship with a company that is providing an adjuvant for the HIV vaccine candidate in the current Phase I clinical trial. In any future clinical development of the vaccine candidate, we may be required either to license that adjuvant, or use a different adjuvant in conjunction with our HIV vaccine technology, in which case we may not be able to utilize some or all of the results of the currently planned trial as part of our clinical data for obtaining FDA approval of a vaccine.

Our agreements with UMMS may require us to make significant expenditures to fund research at the institution relating to developing therapeutic products based on UMMS' s proprietary technologies that have been licensed to us. We estimate that the aggregate amount of these sponsored research expenditures under our current commitments will be approximately \$842,000 for 2006, although a significant portion of those commitments may be assumed by our planned RNAi subsidiary. Our license agreements with UMMS require us to make payments of an aggregate of up to \$94,000 per year to maintain all of our licenses, with such aggregate annual payments increasing to as much as \$154,000 if we are not then conducting certain sponsored research at the institution. We are obligated to pay legal expenses for the prosecution of patents licensed from UMMS. We anticipate that those expenses will be approximately \$250,000 during 2006 and 2007. Our UMMS license agreements also provide, in certain cases, for milestone payments, from us to UMMS, based on the progress we make in the clinical development and marketing of products utilizing the technologies licensed from UMMS. In addition, our license agreements with UMMS require us to reimburse UMMS for legal expenses that they incur in prosecuting and maintaining of the related licenses patents. We estimate these legal expenses to be approximately \$200,000 per year. In the event that we were to successfully develop a product in each of the categories of obesity/type 2 diabetes, ALS, CMV and an HIV vaccine, under our licenses, those milestone payments could aggregate up to \$16.1 million. Those milestone payments, however, could vary significantly based upon the milestones we achieve and the number of products we ultimately undertake to develop. In addition, our collaboration and invention disclosure agreement with UMMS requires us to make payments totaling up to \$375,000 in 2006 in consideration for the option, upon making a specified payment, to negotiate an exclusive worldwide license to certain disclosed technologies.

***Obesity and Type 2 Diabetes***

Obesity and type 2 diabetes are significant health problems. The World Health Organization estimates that, on a worldwide basis, there are more than 300 million cases of obesity and 159 million cases of type 2 diabetes. According to the American Obesity Association, there are currently more than 60 million cases of obesity in the United States, and the American Diabetes Association reports that there are more than 16 million cases of type 2

**Table of Contents**

diabetes in the United States. Scientists in our Worcester laboratory and scientists at UMMS, as part of our strategic alliance, are focused on using cultured adipocytes (fat cells) as a model system for studying the regulation of gene expression involved in adipocyte differentiation and function. This research may lead to the identification of specific drug targets which regulate insulin signaling as well as other metabolic pathways regulating glucose and fatty acids. With this understanding, the program will focus on drug discovery of small molecule therapeutics and, potentially through a newly-created subsidiary, RNAi-based therapeutics for type 2 diabetes (e.g., drugs that act as insulin sensitizers and compounds that alleviate obesity). We believe that RNAi could potentially be a reliable method to selectively inhibit certain genes and their corresponding protein expression in adipocytes.

In May 2004, we licensed from the technology transfer company of the Imperial College of Science, Technology & Medicine, the exclusive rights to intellectual property covering a drug screening method using RIP 140, which is a nuclear hormone co-repressor that is believed to regulate fat accumulation. This proprietary technology is covered by a pending patent application. We paid the licensor a license fee in the form of cash and shares of our common stock, and we will be required to make defined milestone and royalty payments based on sales of products developed using this technology. We believe this license provides us with an important potential drug target in the area of obesity and type 2 diabetes in conjunction with our RNAi gene silencing technology.

In addition, one of the drug candidates acquired from Biorex, iroxadine, was shown to be well tolerated in two Phase I and one Phase II clinical trials and demonstrated significant improvement of vascular function in the brachial artery of hypertensive patients. We plan to evaluate the preclinical efficacy of this drug for two diabetic complications that involve vascular dysfunction, retinopathy and wound healing. If the drug proves to be efficacious in preclinical work and the FDA agrees that it is appropriate to proceed with a Phase II clinical trial, we believe that a Phase II clinical trial for either of these indications could begin in 2007.

Although we initially intend to develop arimoclomol for the treatment of ALS, the drug also showed efficacy in preclinical animal models of diabetes. If efficacy is observed in additional preclinical models, we would also consider beginning a Phase II clinical trial for diabetes in 2007, as arimoclomol has already been tested in two Phase I clinical trials.

***Research and Development Laboratory***

In addition to the obesity and diabetes work being done under our sponsored research agreement with UMMS, our research and development laboratory located in Worcester, Massachusetts is working to develop orally-active small-molecule and RNAi-based drugs for the prevention and treatment of obesity and type 2 diabetes. Our business strategy is to use our portfolio of state of the art drug discovery technologies and our relationships with leading diabetes and obesity researchers to discover and develop first in class medicines to prevent and treat obesity and type 2 diabetes. Utilizing the RNAi target validation technology that we have licensed from UMMS, in combination with state of the art target identification methods, our research and development laboratory is focused on using a structure-based drug discovery approach to accelerate the process of screening and identifying potential proprietary drug targets and pathways for these diseases. Through our laboratory, we are seeking to develop orally-administered drugs that are based on promising targets and pathways that we may be able to identify.

Through our license and sponsored research agreement with UMMS, we have secured rights to novel drug targets believed to be involved in obesity and type 2 diabetes. We will seek to validate these targets using the proprietary high throughput RNAi screening technology that we have licensed from UMMS and will apply state-of-the-art structure-based medicinal chemistry to develop small molecules and RNAi-based therapeutic products.

***Cardiovascular Disease***

Preclinical results by third parties with our drug candidate, iroxadine, indicate that it has therapeutic potential for the treatment of cardiovascular atherosclerosis. If iroxadine proves to be effective in additional preclinical work, we plan to seek a strategic alliance with a larger company to support the subsequent clinical development for this indication.

**Table of Contents****Pre-Global Genomics Merger Technologies**

The following discussion describes our primary scientific programs prior to our merger with Global Genomics on July 19, 2002, and the status of those programs today.

***Therapeutic Copolymer Program***

Before the Global Genomics merger, our primary focus was on CRL-5861 (purified poloxamer 188), which we also call Flocor. Flocor is an intravenous agent for the treatment of sickle cell disease and other acute vaso-occlusive disorders. Sickle cell disease is an inherited disease caused by a genetic mutation of hemoglobin in the blood, and acute vaso-occlusive disorders are a blockage of blood flow caused by deformed, or sickled, red blood cells which can cause intense pain in sickle cell disease patients. In June 2004, we licensed our copolymer technologies, including Flocor, on an exclusive basis, to SynthRx, Inc., a Houston, Texas-based biopharmaceutical company. As a result of the SynthRx license, we received a 19.9% ownership interest in SynthRx and a cash payment from SynthRx of approximately \$228,000, in return for our rights to the licensed technologies. In addition, upon commercialization of any products developed under our alliance with SynthRx, we may also receive significant milestone payments and royalties. Prior to the change in our business strategy that led us to seek licensees for our Flocor technology, we had internally developed Flocor. In December 1999, we reported results from a Phase III clinical study of Flocor for treatment of acute sickle cell crisis. Although the study did not demonstrate statistical significance in the primary endpoint, or objective, of the study, statistically significant and clinically important benefits associated with Flocor were observed in certain subgroups. All amounts paid to us by SynthRx are non-refundable upon termination of the agreement and require no additional effort on our part.

***Vaccine Enhancement and Gene Therapy***

Gene therapy and gene-based vaccines are mediated through the delivery of DNA containing selected genes into cells by a process known as transfection. We refer to our gene delivery technology as TranzFect. A large majority of the revenues we have generated over the past three years has been due to license fees paid to us with respect to our TranzFect technology, representing 54%, 93% and 81% of our total revenues for 2005, 2004 and 2003, respectively.

***Merck License***

In November 2000, we entered into an exclusive, worldwide license agreement with Merck & Co., Inc. whereby we granted Merck the right to use our TranzFect technology in DNA-based vaccines for HIV and three other targets. To date, Merck has focused its efforts on the HIV application, which is still at an early stage of clinical development, and, in July 2003, Merck notified us that it was returning to us the rights to the three other targets covered by its license, which we are now able to license to other third parties. In November 2000, Merck paid us a signature payment of \$2 million. In February 2002, we received an additional \$1 million milestone fee related to the commencement of Merck's first FDA Phase I study for a product incorporating TranzFect designed for the prevention and treatment of HIV. Merck completed a multi-center, blinded, placebo controlled Phase I trial of an HIV vaccine utilizing TranzFect as a component. Although the formulation of this tested vaccine was generally safe, well-tolerated and generated an immune response, the addition of TranzFect to the vaccine did not increase this immune response. Moreover, the DNA single-modality vaccine regimen with TranzFect, when tested in humans, yielded immune responses that were inferior to those obtained with the DNA vaccines in macaque monkeys. All amounts paid to us by Merck are non-refundable upon termination of the agreement and require no additional effort on our part.

***Vical License***

In December 2001, we entered into a license agreement with Vical Incorporated granting Vical exclusive, worldwide rights to use or sublicense our TranzFect poloxamer technology to enhance viral or non-viral delivery of polynucleotides, such as DNA and RNA, in all preventive and therapeutic human and animal health applications, except for (1) the four targets previously licensed by us to Merck, (2) DNA vaccines or therapeutics based on prostate-specific membrane antigen, or PSMA, and (3) sale of a non-regulated product for use as a non-clinical research reagent to increase transfection *in vitro* or in laboratory animals. In addition, the Vical license permits Vical to use TranzFect poloxamer technology to enhance the delivery of proteins in prime-boost vaccine applications that involve the use of polynucleotides (short segments of DNA or RNA). Under the Vical license, we received a non-

**Table of Contents**

refundable up-front payment of \$3,750,000, and, in addition to annual maintenance payments, we have the potential to receive milestone and royalty payments in the future based on criteria described in the agreement. In each of April 2004 and January 2005, we received additional \$100,000 milestone fees related to the commencement of Vical's first FDA Phase I clinical trial for a product incorporating our TranzFect technology. All amounts paid to us by Vical are non-refundable upon termination of the agreement and require no additional effort on our part.

**Genomics Investments**

In connection with our merger with Global Genomics in July 2002, we acquired indirectly equity interests in two development-stage genomics companies, a 40% equity interest in Blizzard and a 5% equity interest in Psynomics. In the fourth quarter of 2003, we decided that we would cease funding our investments in those genomics companies to focus on our core strategy of developing human therapeutics for large market indications. In May 2004, we determined that a write-off of those investments in the third quarter of 2003 should have been made. Our decision to record the write-off was based upon several factors, including Blizzard's lack of success in raising a significant amount of the financing necessary for it to pursue the commercialization strategy for its products, current financial projections prepared by Blizzard, application of a discounted cash flow valuation model of Blizzard's projected cash flows and the consideration of other qualitative factors. Based upon the quantitative and qualitative factors described above, in addition to others, we determined that the investment in Blizzard had no remaining value as of September 30, 2003 and that a write-off of this investment should have been made in the third quarter of 2003. It is our understanding that, by the end of 2003, Blizzard had ceased operations and, in 2004, returned its licensed intellectual property to the Minnesota Research Fund.

**Manufacturing**

We do not have the facilities or expertise to manufacture any of the clinical or commercial supplies of any of our products, including our supply of arimoclomol used for our clinical program. To be successful, our products and the products of our partners must be manufactured in commercial quantities in compliance with regulatory requirements and at an acceptable cost. To date, we have not commercialized any products, nor have we demonstrated that we can manufacture commercial quantities of our product candidates in accordance with regulatory requirements. If we cannot manufacture products in suitable quantities and in accordance with regulatory standards, either on our own or through contracts with third parties, it may delay clinical trials, regulatory approvals and marketing efforts for such products. Such delays could adversely affect our competitive position and our chances of achieving profitability. We cannot be sure that we can manufacture, either on our own or through contracts with third parties, such products at a cost or in quantities, which are commercially viable. We currently rely and intend to continue to rely on third-party contract manufacturers to produce materials needed for research, clinical trials and, ultimately, for product commercialization.

**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 have filed applications for a number of patents and have been granted patents related to technologies, primarily TranzFect and Flocor, we were developing prior to our 2002 merger with Global Genomics. Subsequent to the merger, we acquired patents in connection with our acquisition of intellectual property rights of Biorex and we have licensed additional technologies covered by patents or patent applications, most of which are in the RNAi field.

As part of our development process, we evaluate the patentability of new inventions and improvements developed by us or our collaborators. Whenever appropriate, we will endeavor to file United States and international patent applications to protect these new inventions and improvements. However, 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 United States or any other country. Even if issued, there can be no assurance that those patents will be sufficiently broad to prevent others from using our products or processes. Furthermore, our patents, 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 co-induction and other small



**Table of Contents**

molecule technology, RNAi technology, DNA-based vaccines or other compounds, products or processes competitive with ours.

In addition to patent protection, we also 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. Nevertheless, there can be no assurance that these agreements will afford significant protection against misappropriation or unauthorized disclosure of our trade secrets and confidential information.

**Competition**

Currently, Rilutek<sup>®</sup>, which was developed by Aventis Pharma AG, is the only drug of which we are aware that has been approved by the FDA for the treatment of ALS. Other companies are working to develop pharmaceuticals to treat ALS, including Aeolus Pharmaceuticals, Ono Pharmaceuticals, Trophos SA, FaustPharmaceuticals SA and Oxford BioMedica plc. In addition, ALS belongs to a family of diseases called neurodegenerative diseases, which includes Alzheimer's, Parkinson's and Huntington's disease. Due to similarities between these diseases, a new treatment for one ailment potentially could be useful for treating others. There are many companies that are producing and developing drugs used to treat neurodegenerative diseases other than ALS, including Amgen, Inc., Cephalon, Inc., Ceregene, Inc., Elan Pharmaceuticals, plc, H. Lundbeck A/S, Phytopharm plc, and Schwarz Pharma AG.

The RNAi field, though at an early stage of development, is already a competitive one and the competition is expected to increase. We face competition on many fronts ranging from large and small pharmaceutical, chemical and biotechnology companies to universities, government agencies and other public and private research organizations. Examples of companies that are focusing their commercial efforts in the RNAi field are Sirna Therapeutics, Alnylam Pharmaceuticals, Acuity Pharmaceuticals, Nastech Pharmaceutical Company Inc., Nucleonics, Inc. and Benitec Ltd. A number of the multinational pharmaceutical companies also either have their own gene silencing product development programs or are working with smaller biopharmaceutical companies in this area. In addition to our RNAi competitors, companies in other fields may be using other technologies to target the same diseases that we are targeting. The competition from other firms and institutions will manifest itself not only in our potential product markets but also, and importantly at this stage in development of RNAi technology, in recruiting and retaining key scientific and management personnel.

Companies developing HIV vaccines that could compete with our HIV vaccine technology include Merck, VaxGen, Inc., AlphaVax, Inc. and Immunitor Corporation, and ABL may also seek to develop competing HIV vaccines that could utilize a portion of the technology that we have licensed from UMMS and ABL.

With respect to both our RNAi and non-RNAi products, many companies, including large pharmaceutical and biotechnology firms with financial resources, research and development staffs, and facilities that may, in certain cases, 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.



**Table of Contents****Government Regulation**

The marketing of pharmaceutical products requires the approval of the FDA and comparable regulatory authorities in foreign countries. The FDA has established guidelines and safety standards which apply to the pre-clinical evaluation, clinical testing, manufacture and marketing of pharmaceutical products. The process of obtaining FDA approval for a new drug product generally takes a number of years and involves the expenditure of substantial resources. The steps required before such a product can be produced and marketed for human use in the United States include preclinical studies in animal models, the filing of an Investigational New Drug (IND) application, human clinical trials and the submission and approval of a New Drug Application (NDA) or a Biologics License Application (BLA). The NDA or BLA involves considerable data collection, verification and analysis, as well as the preparation of summaries of the manufacturing and testing processes, preclinical studies, and clinical trials. The FDA must approve the NDA or BLA before the drug may be marketed. There can be no assurance that we or our strategic alliance partners or licensees will be able to obtain the required FDA approvals for any of our products.

The manufacturing facilities and processes for our products, which we anticipate will be manufactured by our strategic partners or licensees or other third parties, will be subject to rigorous regulation, including the need to comply with Federal Good Manufacturing Practice regulations. 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.

**Employees**

As of March 31, 2005, we had 26 employees, 17 of whom were engaged in research and development activities and 9 of whom were involved in management and administrative operations. All of the full-time employees engaged in research and development activities hold Ph.D. degrees.

**RISK FACTORS**

You should carefully consider the following risks before deciding to purchase shares of our common stock. You should also refer to the other information in this prospectus and the information incorporated into this registration statement by reference, including our financial statements and the related notes.

***We Have Operated at a Loss and Will Likely Continue to Operate at a Loss For the Foreseeable Future***

We have incurred significant losses over the past five years, including net losses of \$15.1 million, \$16.4 million and \$17.8 million for the years ended December 31, 2005, 2004 and 2003, respectively, and we had an accumulated deficit of approximately \$121.3 million as of December 31, 2005. Our operating losses have been due primarily to our expenditures for research and development on our products and for general and administrative expenses and our lack of significant revenues. We are likely to continue to incur operating losses until such time, if ever, that we generate significant recurring revenues.

***We Have No Source of Significant Recurring Revenues, Which Makes Us Dependent on Financing to Sustain Our Operations***

Our revenues were \$184,000, \$428,000 and \$94,000 during the years ended December 31, 2005, 2004 and 2003, respectively. We anticipate it will take a minimum of three years (and possibly longer) for us to generate recurring revenues. We will not have significant recurring operating revenues until at least one of the following occurs:

We are able to commercialize one or more of our products in development, which may require us to first enter into license or other arrangements with third parties.

One or more of our licensed products is commercialized by our licensees, thereby generating royalty revenues for us.

We are able to acquire products from third parties that are already being marketed or are approved for marketing.

**Table of Contents**

We will be dependent on obtaining financing until such time, if ever, as we can generate significant recurring revenues. On March 7, 2006, we completed a private placement financing and received net proceeds of approximately \$12.4 million. Although we believe that we have adequate financial resources to support our currently planned level of operations into the third quarter of 2007, we will be dependent on obtaining financing from third parties in order to maintain our operations, including our Phase II clinical program with arimoclomol for ALS, our planned levels of operations for our obesity and type 2 diabetes laboratory, our planned RNAi subsidiary and our ongoing research and development efforts related to our other small molecule drug candidates, and in order to continue to meet our obligations to UMMS.

We have no commitments from third parties to provide us with any additional debt or equity financing, and may not be able to obtain future financing on favorable terms, or at all. A lack of needed financing would force us to reduce the scope of, or terminate, our operations, or to seek to merge with or to be acquired by another company. There can be no assurance that we could complete such a merger or acquisition on terms that would be attractive to our stockholders, or at all.

***Most of Our Revenues Have Been Generated by License Fees for TranzFect, Which May Not be a Recurring Source of Revenue for Us***

License fees paid to us with respect to our TranzFect technology represented 54%, 93% and 81% of our total revenues for the years ended December 31, 2005, 2004 and 2003, respectively. We have licensed most of the potential applications for this technology, and we may not be able to generate any significant additional license fees from this technology. Our current licensees for TranzFect, Merck and Vical, may be required to make further milestone payments to us under their licenses based on their future development of products using TranzFect. Since TranzFect is to be used as a component in vaccines, we do not need to seek FDA approval, but any vaccine manufacturer will need to seek FDA approval for the final vaccine formulation containing TranzFect. Merck has completed a multi-center, blinded, placebo controlled Phase I trial of an HIV vaccine utilizing TranzFect as a component. In the Merck trials, although the formulation of the tested vaccine using TranzFect was generally safe, well-tolerated and generated an immune response, the addition of TranzFect to the vaccine did not increase this immune response. Moreover, the DNA single-modality vaccine regimen with TranzFect, when tested in humans, yielded immune responses that were inferior to those obtained with the DNA vaccines in macaque monkeys. Accordingly, there is likely to be a substantial period of time, if ever, before we receive any further significant payments from Merck or Vical under their TranzFect licenses.

***Our Business Strategy Will Require Us to Rely Upon Third Parties for the Development of Our Products and to Provide Us With Products***

Our business strategy is to enter into strategic alliances, license agreements or other collaborative arrangements with other pharmaceutical companies under which those companies are responsible for the development and marketing of our products. In June 2004, we licensed Flocor, the primary potential product that we held prior to our merger with Global Genomics and which we had not already licensed to a third party, to SynthRx, Inc., a Houston, Texas-based biopharmaceutical company. The completion of the development of our other products, as well as the manufacture and marketing of our products, will require us to enter into strategic arrangements with other pharmaceutical or biotechnology companies.

There can be no assurance that any of our products will 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. We do not have a commercial relationship with the company that provided an adjuvant for the vaccine for the Phase I clinical trial conducted by UMMS and Advanced BioScience Laboratories on an HIV vaccine candidate that utilizes a technology that we licensed from UMMS. If we are not able to enter into such a relationship, we may be unable to use some or all of the results of the clinical trial as part of our clinical data for obtaining FDA approval of this vaccine, which will delay the development of the vaccine.

If 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 regulatory (including FDA)

requirements, the timing of receipt or amount of revenues from these arrangements may be materially and

**Table of Contents**

adversely affected. By entering into these arrangements rather than completing the development and then marketing these products on our own, we may suffer a reduction in the ultimate overall profitability for us of these products. In addition, if we are unable to enter into these arrangements for a particular product, we may be required to either sell our rights in the product to a third party or abandon it unless we are able to raise sufficient capital to fund the substantial expenditures necessary for development and marketing of the product.

We may also seek to acquire products from third parties that already are being marketed or have previously been marketed. We have not yet identified any of these products. Even if we do identify such products, it may be difficult for us to acquire them with our limited financial resources and, if we acquire products using our securities as currency, we may incur substantial shareholder dilution. We do not have any prior experience in acquiring or marketing products and may need to find third parties to market these products for us. We may also seek to acquire products through a merger with one or more companies that own such products. In any such merger, the owners of our merger partner could be issued or hold a substantial, or even controlling, amount of stock in our company or, in the event that the other company is the surviving company, in that other company.

***Our Current Financial Resources May Limit Our Ability to Execute Certain Strategic Initiatives***

In June 2004, we licensed Flocor to SynthRx, which will be responsible for developing potential product applications for Flocor. Although we are not doing any further development work on TranzFect or Flocor, should our three principal licensees for those technologies successfully meet the defined milestones, we could receive future milestone payments and, should any of the licensees commercialize products based upon our technology, future royalty payments. However, there can be no assurance that our licensees will continue to develop or ever commercialize any products that are based on our Flocor or our TranzFect technology.

Our strategic alliance with UMMS will require us to make significant expenditures to fund research at UMMS relating to the development of therapeutic products based on UMMS's technologies that we have licensed and pursuant to our collaboration and invention disclosure agreement with UMMS. We estimate that the aggregate amount of these expenditures under our current commitments will be approximately \$1,186,000 million for 2006 and approximately \$450,000 for 2007. Our license agreements with UMMS also provide, in certain cases, for milestone payments based on the progress we make in the clinical development and marketing of products utilizing the licensed technologies. In the event that we were to successfully develop a product in each of the categories of obesity/type 2 diabetes, ALS, CMV and an HIV vaccine, under our licenses, those milestone payments could aggregate up to \$16.1 million.

We estimate that the Phase II clinical program with arimoclomol for ALS, including the recently-initiated Phase IIa trial and the Phase IIb trial that we expect to initiate soon after completion of the present Phase IIa trial subject to FDA approval, will require us to expend approximately \$17.8 million over a period of 24 to 30 months. In addition, the agreement pursuant to which we acquired the clinical and pharmaceutical assets of Biorex provides for milestone payments based on the occurrence of certain regulatory filings and approvals related to the acquired products. In the event that we successfully develop any of the products acquired from Biorex, the milestone payments could aggregate up to \$4.2 million. Each of the foregoing milestone payments, however, could vary significantly based upon the milestones we achieve and the number of products we ultimately undertake to develop.

Under our license for our HIV vaccine candidate, following the completion of the current Phase I trial, we will be responsible for all of the costs for subsequent clinical trials for this vaccine. The costs of subsequent trials for the HIV vaccine will be very substantial. Although we are seeking NIH or other governmental funding for these future trials, there can be no assurance that we will be able to secure any such funding.

The expenditures potentially required under our agreements with UMMS and ABL, together with the capital requirements of our obesity and type 2 diabetes laboratory and funding needs of our other planned research and development activities, substantially exceed our current financial resources. Although we raised approximately \$12.4 million in March 2006, net of transaction expenses, we will require additional capital or to secure a licensee or strategic partner in order to maintain our operations, including our Phase II clinical program with arimoclomol for ALS, our planned levels of operations for our obesity and type 2 diabetes laboratory, our planned RNAi subsidiary and our ongoing research and development efforts related to our other small molecule drug candidates, and in order to continue to meet our obligations to UMMS. If we are unable to meet our financial obligations under our license agreements with UMMS, we could lose all of our rights under those agreements. If we were to have inadequate



**Table of Contents**

financial resources at that time, we also could be forced to reduce the level of, or discontinue, operations at our laboratory.

***If Our Products Are Not Successfully Developed and Approved by the FDA, We May Be Forced to Reduce or Terminate Our Operations***

All of our products in development must be approved by the FDA or similar foreign governmental agencies before they can be marketed. The process for obtaining FDA approval 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, which may take longer or cost more than we or our licensees 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 products may not necessarily indicate 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 drug 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 the FDA's requirements for our testing during the course of that testing.

Inability to generate statistically significant data confirming the efficacy of the product being tested.

Modification of the drug during testing.

Reallocation of our limited financial and other resources to other clinical programs.

It is possible that none of the products we develop will obtain the appropriate regulatory approvals necessary for us to begin selling them. The time required to obtain FDA and other approvals is unpredictable but often can take years following the commencement of clinical trials, depending upon the complexity of the drug candidate. Any analysis we perform of data from clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent regulatory approval. Any delay or failure in obtaining required approvals could have a material adverse effect on our ability to generate revenues from the particular drug candidate.

***The Approach We Are Taking to Discover and Develop Novel Therapeutics Using RNAi is Unproven and May Never Lead to Marketable Products***

The RNAi technologies that we have acquired from UMMS have not yet been clinically tested by us, nor are we aware of any clinical trials having been completed by third parties involving similar technologies. Neither we nor any other company has received regulatory approval to market therapeutics utilizing RNAi. The scientific discoveries that form the basis for our efforts to discover and develop new drugs are relatively new. The scientific evidence to support the feasibility of developing drugs based on these discoveries is both preliminary and limited. Successful development of RNAi-based products will require solving a number of issues, including providing suitable methods of stabilizing the RNAi drug material and delivering it into target cells in the human body. We may spend large amounts of money trying to solve these issues, and never succeed in doing so. In addition, any compounds that we develop may not demonstrate in patients the chemical and pharmacological properties ascribed

**Table of Contents**

to them in laboratory studies, and they may interact with human biological systems in unforeseen, ineffective or even harmful ways.

***Our Planned RNAi Subsidiary May Not Be Able to Obtain Sufficient Funding, and We May Not Control a Majority of the Planned Subsidiary if We Obtain Financing***

We are currently pursuing a plan to transfer all of our RNAi therapeutics assets into a newly-formed subsidiary to accelerate the development and commercialization of drugs based on RNAi technology. Although we believe that this structure may facilitate our obtaining additional financing to pursue our RNAi development efforts, we have no commitments or arrangements for any financing, and there is no assurance that we will be able to obtain financing for this purpose. Our planned RNAi subsidiary will be only partially owned by us. Depending upon the amount and terms of its future financing activities, we may not control the subsidiary, or may share control with other shareholders whose interests may not be directly aligned with ours. It also is possible that any products developed by the RNAi subsidiary could eventually compete with our products for some disease indications, such as ALS, type 2 diabetes and obesity.

***The Drug Candidates Acquired from Biorex May Not Obtain Regulatory Marketing Approvals***

On October 4, 2004, we acquired all of the clinical and pharmaceutical assets and related intellectual property of Biorex, including three drug candidates (arimoclomol, irovanadine and bimoclomol), and a library of small molecule drug candidates. Although each of arimoclomol, irovanadine and bimoclomol has undergone clinical testing, significant and costly additional testing will be required in order to bring any product to market. We may be unable to confirm in our pre-clinical or clinical trials with arimoclomol, irovanadine or bimoclomol the favorable pre-clinical or clinical data previously generated by European investigators for these drug candidates, which could require us to have to modify our development plans for these compounds.

In September 2005, we initiated Phase II clinical testing for arimoclomol for ALS. There is no assurance that the clinical testing will be successful, or that the FDA will permit us to commence our planned Phase IIb clinical trial upon the completion of our ongoing Phase IIa clinical trial. Any additional requirements imposed by the FDA in connection with the ongoing Phase IIa trial, or in connection with our planned Phase IIb trial, could add further time and expense for us to carry out this trial.

We believe that the FDA may accept the completion of a successful Phase II clinical program as sufficient to enable us to submit a New Drug Application, or NDA; however, there is no assurance that the FDA will accept our Phase II program in lieu of a Phase III clinical trial. If the FDA requires us to complete a Phase III clinical trial, the cost of development of arimoclomol will increase significantly beyond our estimated costs, and the time to completion of clinical testing will be delayed. In addition, the FDA ultimately could require us to achieve an efficacy end point in the clinical trials for arimoclomol that could be more difficult, expensive and time-consuming than our planned end point. Although we anticipate developing arimoclomol for the treatment of ALS, arimoclomol has also shown therapeutic efficacy in a preclinical animal model of diabetes and we may pursue development of arimoclomol for diabetic indications. However, such development would require significant and costly additional testing. There is no guarantee that arimoclomol will show any efficacy for any indication.

Irovanadine has been tested in two Phase I clinical trials and one Phase II clinical trial which indicated improvement in the function of endothelial cells in blood vessels of patients at risk of cardiovascular disease. We intend to develop this product to improve endothelial dysfunction in indications such as diabetic retinopathy and wound healing, which will require significant and costly additional testing. There is no guarantee that irovanadine will show any efficacy in the intended uses we are seeking. We may also attempt to license irovanadine to larger pharmaceutical or biotechnology companies for cardiovascular indications; however, there is no guarantee that any such company will be interested in licensing irovanadine from us or licensing it on terms that are attractive to us.

Bimoclomol has been tested in two Phase II clinical trials where it was shown to be safe, but where it did not show efficacy for diabetic neuropathy, the indication for which it was tested. We intend to develop this compound for other therapeutic indications; however, there can be no guarantee that this compound will be effective in treating any diseases. In addition, the FDA may require us to perform new safety clinical trials, which would be expensive and time consuming and would delay development of bimoclomol.





**Table of Contents**

There is no guarantee that any additional clinical trials will be successful or that the FDA will approve any of these products and allow us to begin selling them in the United States.

***Our Obesity and Type 2 Diabetes Laboratory May Not Be Able to Develop Products***

In order to develop new obesity and type 2 diabetes products, we will first need to identify appropriate drug targets and pathways. We are using novel RNAi-based techniques to accelerate this process, but there is no assurance that these techniques will accelerate our work or that we will be able to identify promising targets or pathways using these techniques or otherwise. Even if we are successful in identifying these targets or pathways, we will need to then develop proprietary molecules that are safe and effective against these targets. The development process and the clinical testing of our potential products will take a lengthy period of time and involve expenditures substantially in excess of our current financial resources available for this purpose. We are currently seeking a strategic alliance with a major pharmaceutical or biotechnology company to complete the development, clinical testing and manufacturing and marketing of our potential obesity and type 2 diabetes products, which are at an early stage of development, but we may not be able to secure such a strategic partner on attractive terms, or at all. We do not have prior experience in operating a genomic and proteomic-based drug discovery company. Accordingly, we will be heavily dependent on the prior experience and current efforts of Dr. Michael P. Czech, the Chairman of our Scientific Advisory Board, Dr. Jack Barber, our Senior Vice President Drug Development, and Dr. Mark A. Tepper, our Senior Vice President Drug Discovery, in establishing our scientific goals and strategies.

***We Will Be Reliant Upon SynthRx to Develop and Commercialize Flocor***

In June 2004, we licensed Flocor and our other co-polymer technologies to SynthRx and acquired a 19.9% equity interest in that newly formed biopharmaceutical company. SynthRx has only limited financial resources and will have to either raise significant additional capital or secure a licensee or strategic partner to complete the development and commercialization of Flocor and these other technologies. We are not aware that SynthRx has any commitments from third parties to provide the capital that it will require, and there can be no assurance that it will be able to obtain this capital or a licensee or strategic partner on satisfactory terms, or at all.

Our prior Phase III clinical trial of Flocor for the treatment of sickle cell disease patients experiencing an acute vaso-occlusive crisis did not achieve its primary objective. However, in this study, for patients 15 years of age or younger, the number of patients achieving a resolution of crisis was higher for Flocor-treated patients at all time periods than for placebo-treated patients, which may indicate that future clinical trials should focus on juvenile patients. Generating sufficient data to seek FDA approval for Flocor will require additional clinical studies, which have not yet been funded or commenced by SynthRx, and, if undertaken, those studies would entail substantial time and expense for SynthRx.

The manufacture of Flocor involves obtaining new raw drug substance and a supply of the purified drug from the raw drug substance, which requires specialized equipment. Should SynthRx encounter difficulty in obtaining the purified drug substance in sufficient amounts and at acceptable prices, SynthRx may be unable to complete the development or commercialization of Flocor on a timely basis, or at all.

***We Are Subject to Intense Competition and There is No Assurance that We Can Compete Successfully***

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

As a result, these competitors may:

Succeed in developing competitive products sooner than us or our strategic partners or licensees.

**Table of Contents**

Obtain FDA and other regulatory approvals for their products before we can obtain approval of any of our products.

Obtain patents that block or otherwise inhibit the development and commercialization of our product candidates.

Develop products that are safer or more effective than our products.

Devote greater resources to marketing or selling their products.

Introduce or adapt more quickly to new technologies and other scientific advances.

Introduce products that render our products obsolete.

Withstand price competition more successfully than us or our strategic partners or licensees.

Negotiate third-party strategic alliances or licensing arrangements more effectively.

Take advantage of other opportunities more readily.

A number of medical institutions and pharmaceutical companies are seeking to develop products based on gene silencing technologies. Companies working in this area include Sirna Therapeutics, Alnylam Pharmaceuticals, Acuity Pharmaceuticals, Natestch Pharmaceutical Company Inc., Nucleonics, Inc., Benitec Ltd. and a number of the multinational pharmaceutical companies. A number of products currently are being marketed by a variety of the multinational or other pharmaceutical companies for treating type II diabetes, including among others the diabetes drugs Avandia<sup>®</sup> by Glaxo SmithKline PLC, Actos<sup>®</sup> by Eli Lilly & Co., Glucophage<sup>®</sup> by Bristol-Myers Squibb Co., Symlin<sup>®</sup> by Amylin Pharmaceuticals, Inc. and Starlix<sup>®</sup> by Novartis and the obesity drugs Acomplia<sup>®</sup> by Sanofi-Aventis SA, Xenical<sup>®</sup> by F. Hoffman-La Roche Ltd. and Meridia<sup>®</sup> by Abbott Laboratories. Many major pharmaceutical companies are also seeking to develop new therapies for these disease indications. Companies developing HIV vaccines that could compete with our HIV vaccine technology include Merck, VaxGen, Inc., AlphaVax, Inc. and Immunitor Corporation.

Currently, Rilutek<sup>®</sup>, which was developed by Aventis Pharma AG, is the only drug of which we are aware that has been approved by the FDA for the treatment of ALS. Other companies are working to develop pharmaceuticals to treat ALS, including Aeolus Pharmaceuticals, Ono Pharmaceuticals, Trophos SA, FaustPharmaceuticals SA and Oxford BioMedica plc. In addition, ALS belongs to a family of diseases called neurodegenerative diseases, which includes Alzheimer's, Parkinson's and Huntington's disease. Due to similarities between these diseases, a new treatment for one ailment potentially could be useful for treating others. There are many companies that are producing and developing drugs used to treat neurodegenerative diseases other than ALS, including Amgen, Inc., Cephalon, Inc., Ceregene, Inc., Elan Pharmaceuticals, plc, H. Lundbeck A/S, Phytopharm plc, and Schwarz Pharma AG.

Although we do not expect Flocor to have direct competition from other products currently available or that we are aware of that are being developed related to Flocor's ability to reduce blood viscosity in the cardiovascular area, there are a number of anticoagulant products that Flocor would have to compete against, such as tissue plasminogen activator, or t-PA, and streptokinase (blood clot dissolving enzymes) as well as blood thinners such as heparin and coumatin. In the sickle cell disease area, Flocor would compete against other products such as Droxia<sup>®</sup> (hydroxyurea) marketed by Bristol-Myers Squibb Co. and Dacogen<sup>™</sup>, which is being developed by SuperGen, Inc. Our TranzFect technology will compete against a number of companies that have developed adjuvant products, such as the adjuvant QS-21<sup>™</sup> marketed by Antigenics, Inc. and adjuvants marketed by Corixa Corp.

***We Do Not Have the Ability to Manufacture Any of Our Products and Will Need to Rely upon Third Parties for the Manufacture of Our Clinical and Commercial Product Supplies***

We do not currently have the facilities or expertise to manufacture any of the clinical or commercial supplies of any of our products, including the supply of arimoclomol used in our Phase II clinical trials. Accordingly, we are and

will be dependent upon contract manufacturers or our strategic alliance partners to manufacture these supplies,

**Table of Contents**

or we will need to acquire the ability to manufacture these supplies ourselves, which could be very difficult, time-consuming and costly. We have a manufacturing supply arrangement in place with respect to the clinical supplies for both the Phase IIa and Phase IIb trials for arimoclomol for ALS. We do not otherwise have manufacturing supply arrangements for our other product candidates, with the exception of an arrangement for clinical supplies for the current Phase I trial of the HIV vaccine product that utilizes the HIV vaccine technology that we have licensed from UMMS. There can be no assurance that we will be able to secure needed manufacturing supply arrangements on attractive terms, or at all. Delays in, or a failure to, secure these arrangements could have a materially adverse effect on our ability to complete the development of our products or to commercialize them.

***We May Be Unable to Protect Our Intellectual Property Rights, Which Could Adversely Affect the Value of Our Assets***

We believe that obtaining and maintaining patent and other intellectual property rights for our technologies and potential products is critical to establishing and maintaining the value of our assets and our business. Although we believe that we have significant patent coverage for the technologies that we acquired from Biorex and for our TranzFect technologies, there can be no assurance that this coverage will be broad enough to prevent third parties from developing or commercializing similar or identical technologies, that the validity of our patents will be upheld if challenged by third parties or that our technologies will not be deemed to infringe the intellectual property rights of third parties. In particular, although we conducted certain due diligence regarding the patents and patent applications acquired from Biorex and received certain representations and warranties from Biorex in connection with the acquisition, the patents and patent applications acquired from Biorex were issued or filed, as applicable, prior to our acquisition and thus there can be no assurance that the validity, enforceability and ownership of those patents and patent applications will be upheld if challenged by third parties. We have a nonexclusive license to a patent owned by UMMS and the Carnegie Institution of Washington that claims various aspects of gene silencing, or genetic inhibition by double-stranded RNA, but there can be no assurance that this patent will withstand possible third-party challenges or otherwise protect our technologies from competition. The medical applications of the gene silencing technology and the other technologies that we have licensed from UMMS also are claimed in a number of pending patent applications, but there can be no assurance that these applications will result in any issued patents or that those patents would withstand challenges or protect our technologies from competition. Moreover, we are aware of at least one other issued United States patent claiming broad applications for RNAi, and many patent applications covering different methods and compositions in the field of RNAi therapeutics have been and are expected to be filed, and certain organizations or researchers may hold or seek to obtain patents that could make it more difficult or impossible for us to develop products based on the gene silencing technology that we have licensed. We are aware that at least one of our competitors is seeking patent coverage in the RNAi field that could restrict our ability to develop certain RNAi-based therapeutics.

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

We are sponsoring research at UMMS and Massachusetts General Hospital under agreements that give us certain rights to acquire licenses to inventions, if any, that arise from that research, and we may enter into additional research agreements with those institutions, or others, in the future. We also have a collaboration and invention disclosure agreement with UMMS under which UMMS has agreed to disclose to us certain inventions it makes and to give us an option to negotiate licenses to the disclosed technologies. There can be no assurance, however, that any such inventions will arise, that we will be able to acquire licenses to any inventions under satisfactory terms or at all, or that any licenses will be useful to us commercially.

***We May Incur Substantial Costs from Future Clinical Testing or Product Liability Claims***

If any of our products are alleged to be defective, they may expose us to claims for personal injury by patients in clinical trials of our products or by patients using our commercially marketed products. Even if the commercialization

of one or more of our products is approved by the FDA, users may claim that such products caused unintended adverse effects. We currently do not carry product liability insurance covering the commercial

**Table of Contents**

marketing of these products. We have obtained clinical trial insurance for our recently-initiated Phase IIa clinical trial with arimocloamol for the treatment of ALS and will seek to obtain such insurance for any other clinical trials that we conduct, including the planned Phase IIb clinical trial for arimocloamol, as well as liability insurance for any products that we market, although there can be no assurance that we will be able to obtain additional insurance in the amounts we seek, or at all. We anticipate that our licensees who are developing our products will carry liability insurance covering the clinical testing and marketing of those products. However, there is no assurance, however, that any insurance maintained by us or our licenses will prove adequate in the event of a claim against us. Even if claims asserted against us are unsuccessful, they may divert management's attention from our operations and we may have to incur substantial costs to defend such claims.

***Compliance with Requirements of Section 404 of the Sarbanes-Oxley Act of 2002 Will Increase Our Costs and Require Additional Management Resources, and We May Not Successfully Comply***

As directed by Section 404 of the Sarbanes-Oxley Act of 2002, the SEC adopted rules requiring public companies to include a report of management on the company's internal controls over financial reporting in their annual reports on Form 10-K. In addition, the independent registered public accounting firm auditing the company's financial statements must attest to and report on management's assessment of the effectiveness of the company's internal controls over financial reporting. The SEC has postponed the effectiveness of this requirement several times; however, if the SEC does not postpone or otherwise alter the requirement again, then we expect that it will first apply to our annual report on Form 10-K for our fiscal year ending December 31, 2006. If we are required to comply, we will incur significant legal, accounting, and other expenses and compliance will occupy a substantial amount of time of our board of directors and management. Uncertainty exists regarding our ability to comply with these requirements by the SEC's current deadlines. If we are unable to complete the required assessment as to the adequacy of our internal control reporting or if we conclude that our internal controls over financial reporting are not effective or if our independent registered public accounting firm is unable to provide us with an unqualified report as to the effectiveness of our internal controls over financial reporting, investors could lose confidence in the reliability of our financial reporting. In addition, while we plan to expand our staff to assist in complying with the additional requirements when and if they become applicable, we may encounter substantial difficulty attracting qualified staff with requisite experience due to the high level of competition for experienced financial professionals.

***Our Anti-Takeover Provisions May Make It More Difficult to Change Our Management or May Discourage Others From Acquiring Us and Thereby Adversely Affect Stockholder Value***

We have a stockholder rights plan and provisions in our bylaws that may discourage or prevent a person or group from acquiring us without the approval of our board of directors. The intent of the stockholder rights plan and our bylaw provisions is to protect our stockholders' interests by encouraging anyone seeking control of our company to negotiate with our board of directors.

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

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

the foregoing bylaw provisions may also make our existing management less responsive to the views

**Table of Contents**

of our stockholders with respect to our operations and other issues such as management selection and management compensation.

***Our Outstanding Options and Warrants and the Registrations of Our Shares Issued in the Global Genomics Merger and Our Recent Private Financings May Adversely Affect the Trading Price of Our Common Stock***

As of December 31, 2005, there were outstanding stock options and warrants to purchase approximately 24.7 million shares of our common stock at exercise prices ranging from \$0.20 to \$2.73 per share. Our outstanding options and warrants could adversely affect our ability to obtain future financing or engage in certain mergers or other transactions, since the holders of options and warrants can be expected to exercise them at a time when we may be able to obtain additional capital through a new offering of securities on terms more favorable to us than the terms of outstanding options and warrants. For the life of the options and warrants, the holders have the opportunity to profit from a rise in the market price of our common stock without assuming the risk of ownership. To the extent the trading price of our common stock at the time of exercise of any such options or warrants exceeds the exercise price, such exercise will also have a dilutive effect on our stockholders. In addition, warrants issued in connection with our financings in 2003 contain anti-dilution provisions that are triggered upon certain events, including any issuance of securities by us below the market price. In the event that those anti-dilution provisions are triggered by us in the future, we would be required to reduce the exercise price, and increase the number of shares underlying, those warrants, which would have a dilutive effect on our stockholders.

In August 2003, we registered with the SEC for resale by the holders a total of 14,408,252 shares of our outstanding common stock and an additional 3,848,870 shares of our common stock issuable upon exercise of outstanding options and warrants, which shares and options and warrants were issued primarily in connection with our merger with Global Genomics and the \$5.4 million private equity financing that we completed in May 2003. In December 2003, we registered a total of 6,113,448 shares of our common stock, consisting of the 5,175,611 shares issued, or that are issuable upon exercise of the warrants issued, in connection with the \$8.7 million private equity financing that we completed in September 2003, and an additional 937,837 shares of our common stock that we issued, or that are issuable upon the exercise of warrants that we issued, to certain other third parties. In November 2004, we registered 4,000,000 shares of our common stock and an additional 3,080,000 shares of our common stock issuable upon the exercise of warrants in connection with the \$4,000,000 private equity financing that we completed in October 2004, and an additional 1,550,000 shares of our common stock issued or issuable upon exercise of warrants to other third parties. In February 2005, we registered 17,334,494 shares of our common stock and an additional 9,909,117 shares of our common stock issuable upon the exercise of warrants in connection with the \$21.3 million private equity financing that we completed in January 2005. This prospectus covers a total of 17,121,750 shares of our common stock, including the 15,976,194 shares we issued or that are issuable upon exercise of the warrants that we issued to the investors in connection with the \$13.4 million private equity financing in March 2006, and an additional 745,556 shares of our common stock that are issuable to T.R. Winston & Company, LLC, upon the exercise of warrants issued in connection with that financing. Both the availability for public resale of these various shares and the actual resale of these shares could adversely affect the trading price of our common stock. ***We May Issue Preferred Stock in the Future, and the Terms of the Preferred Stock May Reduce the Value of Our Common Stock***

We are authorized to issue up to 5,000,000 shares of preferred stock in one or more series. Our board of directors may determine the terms of future preferred stock offerings without further action by our stockholders. If we issue preferred stock, it could affect your rights or reduce the value of our outstanding common stock. In particular, specific rights granted to future holders of preferred stock may include voting rights, preferences as to dividends and liquidation, conversion and redemption rights, sinking fund provisions, and restrictions on our ability to merge with or sell our assets to a third party.

***Changes in Stock Option Accounting Rules May Adversely Impact Our Reported Operating Results, Our Stock Price and Our Competitiveness in the Employee Marketplace***

In December 2004, the Financial Accounting Standards Board published new rules that will require companies in 2006 to record all stock-based employee compensation as an expense. The new rules apply to stock options grants, as well as a range of other stock-based compensation arrangements, including restricted share plans,





**Table of Contents**

performance-based awards, share appreciation rights, and employee share purchase plans. We will have to apply the new financial accounting rules beginning in the first quarter of 2006. We have depended in the past upon compensating our officers, directors, employees and consultants with such stock-based compensation awards in order to limit our cash expenditures and to attract and retain officers, directors, employees and consultants. Accordingly, if we continue to grant stock options or other stock-based compensation awards to our officers, directors, employees, and consultants after the new rules apply to us, our future earnings, if any, will be reduced (or our future losses will be increased) by the expenses recorded for those grants. The expenses we may have to record as a result of future options grants may be significant and may materially negatively affect our reported financial results. The adverse effects that the new accounting rules may have on our future financial statements should we continue to rely heavily on stock-based compensation may reduce our stock price and make it more difficult for us to attract new investors. In addition, reducing our use of stock plans to reward and incentivize our officers, directors and employees could result in a competitive disadvantage to us in the employee marketplace.

***We May Experience Volatility in Our Stock Price, Which May Adversely Affect the Trading Price of Our Common Stock***

The market price of our common stock has ranged from \$0.21 to \$3.74 per share over the past three years, and may continue to experience significant volatility from time to time. Factors such as the following may affect such volatility:

Our quarterly operating results.

Announcements of regulatory developments or technological innovations by us or our competitors.

Government regulation of drug pricing.

Developments in patent or other technology ownership rights.

Public concern regarding the safety of our products.

Other factors which may affect our stock price are general changes in the economy, the financial markets or the pharmaceutical or biotechnology industries.

**USE OF PROCEEDS**

We will bear the costs and expenses of registering the shares offered by the selling securityholders. Other than the exercise price of the warrants described herein (to the extent they may be exercised), we will not receive any of the proceeds from the sale of the shares offered by the selling securityholders. The holders of the warrants are not obligated to exercise the warrants, and there can be no assurance that they will choose to do so. The warrants may be exercised for cash or pursuant to the cashless exercise provisions contained therein. If the warrants are exercised, in full, for cash, we will receive approximately \$9,349,000 upon exercise.

We intend to use any proceeds we receive from the exercise of the warrants for working capital and general corporate purposes.

**Table of Contents****SELLING SECURITYHOLDERS****Selling Securityholder Table**

The following table sets forth certain information regarding the ownership of our common stock by the selling security holders as of March 31, 2006. Beneficial ownership is determined in accordance with the rules of the SEC and generally includes voting or investment power with respect to securities. The percentage ownership reflected in the table is based on 70,457,988 shares of our common stock outstanding as of March 31, 2006, plus in the case of each selling securityholder, the shares issuable upon exercise of any warrants, options or convertible securities held by such selling securityholder (which are indicated by footnote) that are exercisable or convertible within 60 days of March 31, 2006, but not including shares issuable upon exercise or conversion of any other options, warrants or other securities held by any other person. Except as otherwise indicated, to our knowledge, each selling securityholder has sole voting and investment power with respect to the shares of common stock shown. For purposes of the following table, we have assumed that the selling securityholders will sell all the shares of our common stock being offered pursuant to this prospectus. An asterisk denotes beneficial ownership of less than 1%.

	<b>Beneficial Ownership Before Offering</b>	<b>Number of Shares Being Offered</b>	<b>Beneficial Ownership After Offering</b>	
	<b>Number of Shares</b>		<b>Number of Shares</b>	<b>Percent</b>
Alpha Capital AG	818,697(1)	595,238	223,459	*
Bristol Investment Fund, Ltd.	3,515,709(2)	2,380,953	1,134,756	1.6
Capital Ventures International	1,488,095(3)	1,488,095	0	0
D3 LifeScience Ltd.	166,667(4)	166,667	0	0
D3 LifeScience Market Neutral Ltd.	238,095(5)	238,095	0	0
D3 LifeScience Select Ltd.	190,476(6)	190,476	0	0
Emerson Family Foundation	307,143(7)	307,143	0	0
Emerson Partners	345,536(8)	345,536	0	0
Enable Growth Partners LP	875,785(9)	869,049	6,736	0
Enable Opportunity Partners LP	142,858(10)	142,858	0	0
Excalibur Limited Partnership	1,177,410(11)	892,857	284,553	0
High Tide, LLC	148,965(12)	148,965	0	0
Iroquois Master Fund Ltd.	1,309,524(13)	1,309,524	0	0
JMG Capital Partners, LP	892,857(14)	892,857	0	0
JMG Triton Offshore Fund, Ltd.	892,857(15)	892,857	0	0
MM & B Holdings	595,238(16)	595,238	0	0
Nite Capital, LP	798,491(17)	595,238	203,253	*
Pierce Diversified Strategy Master Fund LLC	178,573(18)	178,573	0	0
RHP Master Fund, Ltd.	1,190,476(19)	1,190,476	0	0
G. Tyler Runnels or Jasmine Niklas Runnels TTEES The Runnels Family Trust				
DTD 1-11-2000	148,965(20)	148,965	0	0
SDS Capital Group SPC, Ltd.	1,488,096(21)	1,488,096	0	0
Tarek Souki	25,581(22)	25,581	0	0
Whalehaven Capital Fund Limited	1,160,459(23)	892,857	267,602	*
T.R. Winston & Company, LLC	745,556(24)	745,556	0	0
Michael P. Czech	650,000	300,000	350,000	*
Troy & Gould Professional Corporation	107,072(25)	100,000	7,072	*

- (1) Includes 421,872 shares issuable upon exercise of warrants, including 198,413 warrant shares being offered pursuant to this prospectus. Konrad Ackerman has voting and investment control over these securities. Mr. Ackerman disclaims beneficial ownership of these securities.
  
- (2) Includes 1,928,407 shares issuable upon exercise of warrants, including 793,651 warrant shares being offered pursuant to this prospectus. Bristol Capital Advisors, LLC ( BCA ) is the investment advisor to Bristol Investment Fund, Ltd. ( Bristol ). Paul Kessler is the manager of BCA and as such has voting and investment control over the securities held

by Bristol.  
Mr. Kessler  
disclaims  
beneficial  
ownership of  
such securities.

- (3) Includes  
496,032 shares  
issuable upon  
exercise of  
warrants.  
Heights Capital  
Management,  
Inc. is the  
authorized agent  
of Capital  
Ventures  
International.  
Martin  
Kobinger is the  
Investment  
Manager, and as

**Table of Contents**

such has voting and investment control over these securities. Mr. Kobinger disclaims beneficial ownership of these securities.

(4) Includes 55,556 shares issuable upon exercise of warrants. Dr. Fariba Ghodsian is a managing member of the investment manager, D3Capital Management, LLC on behalf of D3 LifeScience Ltd., and as such has voting and investment control over these securities. Dr. Ghodsian disclaims beneficial ownership of these securities.

(5) Includes 79,365 shares issuable upon exercise of warrants. Dr. Fariba Ghodsian is a managing member of the investment manager, D3Capital Management, LLC on behalf of D3 LifeScience Market Neutral Ltd., and as such has voting and investment control over

these securities.  
Dr. Ghodsian  
disclaims  
beneficial  
ownership of  
these securities.

- (6) Includes 63,492  
shares issuable  
upon exercise of  
warrants.  
Dr. Fariba  
Ghodsian is a  
managing  
member of the  
investment  
manager,  
D3Capital  
Management,  
LLC on behalf  
of D3  
LifeScience  
Select Ltd., and  
as such has  
voting and  
investment  
control over  
these securities.  
Dr. Ghodsian  
disclaims  
beneficial  
ownership of  
these securities.

- (7) Includes  
102,381 shares  
issuable upon  
exercise of  
warrants. J.  
Steven Emerson  
has voting and  
investment  
control over  
these securities.  
Excludes 5,000  
shares held  
separately by  
Mr. Emerson.

- (8) Includes  
115,179 shares

issuable upon exercise of warrants. J. Steven Emerson has voting and investment control over these securities. Excludes 5,000 shares held separately by Mr. Emerson.

(9) Includes 296,419 shares issuable upon exercise of warrants, including 289,683 warrant shares being offered pursuant to this prospectus. Mitch Levine, Managing Partner, has voting and investment control over these securities. Mr. Levine disclaims beneficial ownership of these securities.

(10) Includes 47,619 shares issuable upon exercise of warrants. Mitch Levine, Managing Partner, has voting and investment control over these securities. Mr. Levine disclaims beneficial



ownership of  
these securities.

- (11) Includes 582,172 shares issuable upon exercise of warrants, including 297,619 warrant shares offered pursuant to this prospectus. Will Hechter, President of the General Partner of Excalibur Limited Partnership, has voting and investment control over these securities. Mr. Hechter disclaims beneficial ownership of these securities.
- (12) Includes 49,655 shares issuable upon exercise of warrants. G. Tyler Runnels is manager of High Tide, LLC, and as such has voting and investment control over these securities. Mr. Runnels disclaims beneficial ownership of these securities.
- (13) Includes 436,508 shares issuable upon exercise of

warrants. Joshua Silverman has voting and investment control over these securities. Mr. Silverman disclaims beneficial ownership of these securities.

(14) Includes 297,619 shares issuable upon exercise of warrants. The general partner of JMG Capital Partners, L.P. is JMG Capital Management, LLC, which is owned by JMG Capital Management, Inc. and Asset Alliance Holding Corp. Jonathan M. Glaser is the Executive Officer and Director of JMG Capital Management, Inc. and has sole investment discretion over the shares shown.

(15) Includes 297,619 shares issuable upon exercise of warrants. Pacific Assets Management LLC is the manager of

JMG Triton Offshore Fund, Ltd., which is owned by Pacific Capital Management, Inc. and Asset Alliance Holding Corp. Pacific Capital Management, Inc. is owned by Messrs. Roger Richter, Jonathan M. Glaser and Daniel A. David. Messrs. Glaser and Richter share investment discretion over the shares shown.

- (16) Includes 198,413 shares issuable upon exercise of warrants. Marc Ezralow, as Trustee of the Marc Ezralow 1997 Trust, Bryan Ezralow, as Trustee of the Bryan Ezralow 1994 Trust; and Marshall Ezralow, as Trustee

**Table of Contents**

of the Ezralow Family Trust, the general partner of Elevado Investment Company, are the general partners of MM&B Holdings, and as such share voting and investment control over the shares shown.

- (17) Includes 401,666 shares issuable upon exercise of warrants, including 198,413 warrant shares being offered pursuant to this prospectus. Keith A. Goodman is manager of the general partner of Nite Capital, LP, and as such has voting and investment control over these securities. Mr. Goodman disclaims beneficial ownership of these securities.
- (18) Includes 59,524 shares stock issuable upon exercise of warrants. Mitch Levine is the Managing Partner of Pierce Diversified Strategy Master Fund LLC, and as such has voting and investment control over these securities. Mr. Levine disclaims

beneficial  
ownership of  
these securities.

- (19) Includes 396,825 shares issuable upon exercise of warrants. RHP Master Fund, Ltd. is a party to an investment management agreement with Rock Hill Investment Management, L.P., a limited partnership of which the general partner is RHP General Partner, LLC. Pursuant to such agreements, Rock Hill Investment Management directs the voting and disposition of shares owned by RHP Master Fund. Messrs. Wayne Bloch and Peter Lockhart own all of the interests in RHP General Partner. The aforementioned entities and individuals disclaim beneficial ownership of the shares of our common stock owned by the RHP Master

Fund, Ltd.

- (20) Includes 49,655 shares issuable upon exercise of warrants.
- (21) Includes 496,032 shares issuable upon exercise of warrants. Steve Derby is the sole managing member of SDS Management, LLC, the investment manager of SDS Capital Group SPC, Ltd. As such, Mr. Derby has sole voting and investment control over these securities.
- (22) Includes 8,527 shares issuable upon exercise of warrants.
- (23) Includes 565,221 shares issuable upon exercise of warrants, including 297,619 warrant shares being offered pursuant to this prospectus. Arthur Jones, Jennifer Kelly and Derek Wood, Directors of Whalehaven Capital Fund Limited, have voting and

investment  
control over  
these securities.  
Mr. Jones,  
Ms. Kelly and  
Mr. Wood  
disclaim  
beneficial  
ownership of  
these securities.

- (24) Represents  
745,556 shares  
of our common  
stock issuable  
upon exercise of  
warrants. John  
W. Galuchie,  
Jr., President of  
T.R. Winston &  
Company LLC,  
has voting and  
investment  
control over  
these securities.  
Mr. Galuchie,  
Jr. disclaims  
beneficial  
ownership of  
these securities.

- (25) Includes 7,072  
shares issuable  
upon exercise of  
warrants.

#### **Relationships with Selling Securityholders**

The selling securityholders include certain institutional and other investors who acquired a total of 10,650,795 shares of our common stock and warrants to purchase a total of 5,325,397 shares of our common stock in a private equity financing that we closed in March 2006. Certain of these institutional investors are affiliated with registered broker-dealers, but these investors acquired the securities covered by this prospectus in the ordinary course of business and, at the time of their acquisition of these securities, they had no agreements or understandings with any person, whether directly, or indirectly to distribute these securities. The selling securityholders also include T.R. Winston & Company, LLC, to which we issued warrants to purchase 745,556 shares and paid a placement fee of approximately \$764,400 for placement agent services rendered in connection with the foregoing private equity financing.

All of the foregoing warrants are exercisable at an initial exercise price of \$1.54 per share and will expire, unless exercised, on March 7, 2011. The number of shares purchasable upon exercise of the warrants and the exercise price of the warrants are subject to adjustment in the event of a stock split, reverse stock split or similar transaction.

In February 2005, Troy & Gould Professional Corporation, one of the selling securityholders, purchased from us 100,000 shares of our common stock for \$158,000. In February 2004, that firm purchased 100,000 shares of our

**Table of Contents**

common stock for \$184,000. In October 2003, that firm purchased 25,000 shares of our common stock and warrants to purchase 7,072 shares (as adjusted) of our common stock at a current exercise price of \$2.70 per share for a total of \$52,500. In May 2003, that firm purchased 25,000 shares of our common stock for \$25,000. Troy & Gould Professional Corporation has served as our corporate and securities counsel since July 2002.

On June 30, 2005, we issued 650,000 shares of our common stock, including the 300,000 shares being offered pursuant to this prospectus, to Dr. Michael Czech as part of a transaction in which we purchased Dr. Czech's 5% interest in our prior subsidiary, CytRx Laboratories, Inc., with which we subsequently merged. Dr. Czech is a member of our Scientific Advisory Board.

Other than as set forth above, none of the selling securityholders has had any position, office or other material relationship with us or any of our affiliates within the past three years.

The information in the above table is as of March 31, 2005. Information concerning the selling securityholders may change from time to time and any such changed information will be described in supplements to this prospectus if and as required by applicable SEC rules and regulations.



**Table of Contents**

**PLAN OF DISTRIBUTION**

The purpose of this prospectus is to permit the selling securityholders, if they desire, to dispose of some or all of their shares at such times and at such prices as each may choose. Whether sales of shares will be made, and the timing and amount of any sale made, is within the sole discretion of each selling securityholder. The selling securityholders and their pledgees, assignees and successors-in-interest may, from time to time, sell any or all of their shares of common stock on the Nasdaq Capital Market or any other stock exchange, market or trading facility on which the shares are traded or in private transactions. These sales may be at fixed or negotiated prices. A selling securityholder may use any one or more of the following methods when selling shares:

Ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers.

Block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction.

Purchases by a broker-dealer as principal and resale by the broker-dealer for its account.

An exchange distribution in accordance with the rules of the applicable exchange.

Privately negotiated transactions.

Settlement of short sales entered into after the effective date of the registration statement of which this prospectus is a part.

Broker-dealers may agree with the selling stockholders to sell a specified number of such shares at a stipulated price per share.

Through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise.

A combination of any such methods of sale.

Any other method permitted pursuant to applicable law.

The selling securityholders may also sell shares under Rule 144 under the Securities Act of 1933, as amended, or the Securities Act, if available, rather than under this prospectus.

Broker-dealers engaged by selling securityholders may arrange for other brokers-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the selling securityholders (or, if any broker-dealer acts as agent for the purchaser of shares, from the purchaser) in amounts to be negotiated, but, except as set forth in a supplement to this Prospectus, in the case of an agency transaction not in excess of a customary brokerage commission in compliance with NASDR Rule 2440; and in the case of a principal transaction a markup or markdown in compliance with NASDR IM-2440.

In connection with the sale of the shares, the selling securityholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of our common stock in the course of hedging the positions they assume. The selling securityholders may also sell shares short after the effective date of the registration statement of which this prospectus is a part and may deliver the shares described in this prospectus to close out their short positions, or loan or pledge the common stock to broker-dealers that in turn may sell these shares. The selling securityholders may also enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares described in this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

The selling securityholders and any broker-dealers or agents that are involved in selling the shares may be deemed to be underwriters within the meaning of the Securities Act in connection with such sales. In such event,

27

---

## **Table of Contents**

any commissions received by such broker-dealers or agents and any profit on the resale of the shares purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. Each selling securityholder has informed us that it does not have any written or oral agreement or understanding, directly or indirectly, with any person to distribute the shares being offered by means of this prospectus. In no event shall any broker-dealer receive fees, commissions and markups which, in the aggregate, would exceed eight percent (8%).

We are required to pay certain fees and expenses incurred by us incident to the registration of the shares. We have agreed to indemnify the selling securityholders against certain losses, claims, damages and liabilities, including liabilities under the Securities Act.

Because selling securityholders may be deemed to be underwriters within the meaning of the Securities Act, they will be subject to the prospectus delivery requirements of the Securities Act including Rule 172 thereunder. In addition, any securities covered by this prospectus which qualify for sale pursuant to Rule 144 under the Securities Act may be sold under Rule 144 rather than under this prospectus. There is no underwriter or coordinating broker acting in connection with the proposed sale of the resale shares by the selling securityholders.

We agreed to keep this prospectus effective until the earlier of (i) the date on which the shares may be resold by the selling stockholders without registration and without regard to any volume limitations by reason of Rule 144(k) under the Securities Act or any other rule of similar effect or (ii) all of the shares have been sold pursuant to this prospectus or Rule 144 under the Securities Act or any other rule of similar effect.

The resale shares will be sold only through registered or licensed brokers or dealers if required under applicable state securities laws. In addition, in certain states, the resale shares may not be sold unless they have been registered or qualified for sale in the applicable state or an exemption from the registration or qualification requirement is available and is complied with.

Under applicable rules and regulations under the Securities Exchange Act of 1934, or the Exchange Act, any person engaged in the distribution of the shares being offered by the selling securityholders may not simultaneously engage in market making activities with respect to our common stock for the applicable restricted period, as defined in Regulation M, prior to the commencement of the distribution. In addition, the selling securityholders will be subject to applicable provisions of the Exchange Act and the rules and regulations thereunder, including Regulation M, which may limit the timing of purchases and sales of shares by the selling securityholders or any other person. We will make copies of this prospectus available to the selling securityholders and have informed them of the need to deliver a copy of this prospectus to each purchaser at or prior to the time of the sale.

### **WHERE YOU CAN FIND MORE INFORMATION**

We file annual, quarterly and current reports, proxy statements, and other information with the Securities and Exchange Commission, or SEC. You may read any document that we have filed or will file with the SEC without charge at the public reference facilities maintained by the SEC at its main office located at Room 1024, Judiciary Plaza, 450 Fifth Street, N.W., Washington, D.C. 20549.

For a fee prescribed by the SEC, you may obtain copies of all or any portion of the documents that we file with the SEC from the main office of the Public Reference Section of the SEC at the above address, or by calling the SEC at 1-800-SEC-0330. Our filings are also available to the public from commercial document retrieval services and at the SEC's website at <http://www.sec.gov>. We also maintain a website at [www.cytrx.com](http://www.cytrx.com).

This prospectus constitutes part of a registration statement on Form S-3 filed by us with the SEC under the Securities Act. This prospectus does not contain all of the information contained in the registration statement, and reference is hereby made to the registration statement and related exhibits for information with respect to our company and the shares being offered hereby. Any statements contained herein concerning the provisions of any document are not necessarily complete, and, in such instance, reference is made to the copy of such document filed as an exhibit to the registration statement or otherwise filed with the SEC. Each such statement is qualified in its entirety by such reference.

Our common stock is traded on the Nasdaq Capital Market under the symbol CYTR. Reports, proxy and information statements, and other information concerning us also may be inspected at the offices of the National

**Table of Contents**

Association of Securities Dealers, Inc. located at 1735 K Street, N.W., Washington, D.C. 20006.

**INCORPORATION OF INFORMATION FILED WITH THE SEC**

The SEC allows us to incorporate by reference the information we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be a part of this prospectus, and information that we later file with the SEC will automatically update and supersede this information. We incorporate by reference the following documents:

Our annual report on Form 10-K for the fiscal year ended December 31, 2005 filed on April 3, 2006.

Our current report on Form 8-K filed on April 3, 2006.

Our current report on Form 8-K filed on March 30, 2006.

Our current report on Form 8-K filed on March 8, 2006.

Our current report on Form 8-K filed on March 3, 2006.

The description of our common stock and Series A Junior Participating Preferred Stock Purchase Rights as described in our registration statements filed under Section 12 of the Exchange Act, and any amendment or report filed for the purpose of updating any such description.

Any document that we file with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus and before the termination of this offering. Information in these subsequent filings will be deemed to be incorporated by reference as of the date we make the filing.

You may obtain a copy of these filings from us at no cost by writing or calling us at the following address and telephone number: 11726 San Vicente Blvd., Suite 650 Los Angeles, California 90049, (310) 826-5648, Attention: Corporate Secretary.

**LEGAL MATTERS**

The validity of the shares offered hereby has been passed upon for us by Troy & Gould Professional Corporation, Los Angeles, California. Troy & Gould Professional Corporation owns 100,000 shares of our common stock and warrants to purchase an additional 7,072 shares of our common stock.

**EXPERTS**

The financial statements and schedule incorporated by reference in this prospectus have been audited by BDO Seidman, LLP, an independent registered public accounting firm, to the extent and for the periods set forth in their report incorporated herein by reference, and are incorporated herein in reliance upon such report given upon the authority of said firm as experts in auditing and accounting.

**Table of Contents**

**PART II**  
**INFORMATION NOT REQUIRED IN PROSPECTUS**

**ITEM 14. OTHER EXPENSES OF ISSUANCE AND DISTRIBUTION**

We estimate that the expenses incurred in connection with the distribution described in this Registration Statement will be as set forth below. We will bear all of such expenses. Any commissions, discounts and transfer taxes, if any, attributable to sales of the shares being registered hereunder will be borne by the selling securityholders.

SEC registration fee	\$ 3,600
Accounting fees and expenses	\$ 16,400
Legal fees and expenses	\$ 10,000
Miscellaneous	\$ 5,000
 Total	 \$ 35,000

**ITEM 15. INDEMNIFICATION OF DIRECTORS AND OFFICERS**

Section 102(b)(7) of the Delaware General Corporation Law authorizes a corporation in its certificate of incorporation to eliminate or limit personal liability of directors of the corporation for violations of the directors fiduciary duty of care. However, directors remain liable for breaches of duties of loyalty, failing to act in good faith, engaging in intentional misconduct, knowingly violating a law, paying a dividend or approving a stock repurchase which was illegal under Delaware General Corporation Law Section 174 or obtaining an improper personal benefit. In addition, equitable remedies for breach of fiduciary duty of care, such as injunction or recession, are available.

Our Certificate of Incorporation was amended in 1986 so as to eliminate the personal liability of the members of our board of directors to the fullest extent permitted by law. Specifically, Article Eleven of the Certificate of Incorporation provides as follows:

A director of the corporation shall not be personally liable to the corporation or its stockholders for monetary damages for breach of fiduciary duty as a director, except for liability (i) for any breach of the director's duty of loyalty to the corporation or its stockholders, (ii) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (iii) under Section 174 of the Delaware General Corporation Law, or (iv) for any transaction from which the director derived any improper personal benefit. If the Delaware General Corporation Law is amended after approval by the stockholders of this Article to authorize corporate action further eliminating or limiting the personal liability of directors, then the liability of a director of the corporation shall be eliminated or limited to the fullest extent permitted by the Delaware General Corporation Law as so amended.

Any repeal or modification of the foregoing paragraph by the stockholders of the corporation shall not adversely affect any right or protection of a director of the corporation existing at the time of such repeal or modification.

In addition, our Certificate of Incorporation and By-Laws provide for indemnification of our officers and directors to the fullest extent permitted by law. In particular, Article Nine of the Certificate of Incorporation provides as follows:

The corporation shall, to the fullest extent permitted by Section 145 of the General Corporation Law of the State of Delaware, as the same may be amended and supplemented, indemnify any and all persons whom it shall have power to indemnify under said section from and against any and all of the expenses, liabilities or other matters referred to in or covered by said section, and the indemnification provided for herein shall not be deemed exclusive of any other rights to which those indemnified may be entitled under any By-Law, agreement, vote of stockholders or disinterested directors or otherwise, both as to action in his official capacity and as to action in another capacity while holding such office, and shall continue as to a person who has ceased to be a director, officer, employee or agent and shall inure to the benefit of the heirs, executors and administrators of such a person.

**Table of Contents**

Section 145 of the Delaware General Corporation Law provides as follows:

(a) A corporation shall have power to indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of the corporation) by reason of the fact that the person is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by the person in connection with such action, suit or proceeding if the person acted in good faith and in a manner the person reasonably believed to be in or not opposed to the best interests of the corporation, and, with respect to any criminal action or proceeding, had no reasonable cause to believe the person's conduct was unlawful. The termination of any action suit or proceeding by judgment, order, settlement, conviction, or upon a plea of nolo contendere or its equivalent, shall not, of itself, create a presumption that the person did not act in good faith and in a manner which the person reasonably believed to be in or not opposed to the best interests of the corporation, and, with respect to any criminal action or proceeding, had reasonable cause to believe that the person's conduct was unlawful.

(b) A corporation shall have power to indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the corporation to procure a judgment in its favor by reason of the fact that the person is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise against expenses (including attorneys fees) actually and reasonably incurred by the person in connection with the defense or settlement of such action or suit if the person acted in good faith and in a manner the person reasonably believed to be in or not opposed to the best interests of the corporation and except that no indemnification shall be made in respect of any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or the court in which such action or suit was brought shall determine upon application that, despite the adjudication of liability but in view of all the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses which the Court of Chancery or such other court shall deem proper.

(c) To the extent that a director, officer, employee or agent of a corporation has been successful on the merits or otherwise in defense of any action, suit or proceeding referred to in subsections (a) and (b) of this section, or in defense of any claim, issue or matter therein, he shall be indemnified against expenses (including attorneys fees) actually and reasonably incurred by him in connection therewith.

(d) Any indemnification under subsections (a) and (b) of this section (unless ordered by a court) shall be made by the corporation only as authorized in the specific case upon a determination that indemnification of the director, officer, employee or agent is proper in the circumstances because the person has met the applicable standard of conduct set forth in subsections (a) and (b) of this section. Such determination shall be made (1) by a majority vote of the directors who are not parties to such action, suit or proceeding, even though less than a quorum, or (2) if there are no such directors, or if such directors so direct, by independent legal counsel in a written opinion, or (3) by the stockholders.

(e) Expenses (including attorneys fees) incurred by an officer or director in defending any civil, criminal, administrative or investigative action, suit or proceeding may be paid by the corporation in advance of the final disposition of such action, suit or proceeding upon receipt of an undertaking by or on behalf of such director or officer to repay such amount if it shall ultimately be determined that he is not entitled to be indemnified by the corporation as authorized in this section. Such expenses (including attorneys fees) incurred by other employees and agents may be so paid upon such terms and conditions, if any, as the board of directors deems appropriate.

(f) The indemnification and advancement of expenses provided by, or granted pursuant to, the other subsections of this section shall not be deemed exclusive of any other rights to which those seeking indemnification or advancement of expenses may be entitled under any bylaw, agreement, vote of stockholders or disinterested directors or otherwise, both as to action in his official capacity and as to action in another capacity while holding such office.

**Table of Contents**

(g) A corporation shall have power to purchase and maintain insurance on behalf of any person who is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise against any liability asserted against him and incurred by him in any such capacity, or arising out of his status as such, whether or not the corporation would have the power to indemnify him against such liability under this section.

(h) For purposes of this section, references to the corporation shall include, in addition to the resulting corporation, any constituent corporation (including any constituent of a constituent) absorbed in a consolidation or merger which, if its separate existence had continued, would have had power and authority to indemnify its directors, officers, and employees or agents, so that any person who is or was a director, officer, employee or agent of such constituent corporation, or is or was serving at the request of such constituent corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, shall stand in the same position under this section with respect to the resulting or surviving corporation as he would have with respect to such constituent corporation if its separate existence had continued.

(i) For purposes of this section, references to other enterprises shall include employee benefit plans; references to fines shall include any excise taxes assessed on a person with respect to any employee benefit plan; and references to serving at the request of the corporation shall include any service as a director, officer, employee or agent of the corporation which imposes duties on, or involves services by, such director, officer, employee or agent with respect to an employee benefit plan, its participants or beneficiaries; and a person who acted in good faith and in a manner he reasonably believed to be in the interest of the participants and beneficiaries of an employee benefit plan shall be deemed to have acted in a manner not opposed to the best interests of the corporation as referred to in this section.

(j) The indemnification and advancement of expenses provided by, or granted pursuant to, this section shall, unless otherwise provided when authorized or ratified, continue as to a person who has ceased to be a director, officer, employee or agent and shall inure to the benefit of the heirs, executors and administrators of such a person.

(k) The Court of Chancery is hereby vested with exclusive jurisdiction to hear and determine all actions for advancement of expenses or indemnification brought under this section or under any bylaw, agreement, vote of stockholders or disinterested directors, or otherwise. The Court of Chancery may summarily determine a corporation's obligation to advance expenses (including attorneys fees).

Article Five of our By-Laws provides as follows:

1. *Mandatory Indemnification.* The corporation shall indemnify, to the fullest extent permissible under Delaware law, any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative, including an action or suit by or in the right of the corporation to procure a judgment in its favor, by reason of the fact that he or she is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by him in connection with such action, suit or proceeding if he acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interest of the corporation, and, with respect to any criminal action or proceeding, had no reasonable cause to believe his conduct was unlawful.

2. *Mandatory Advancement of Expenses.* Expenses reasonably and actually incurred by a director, officer, employee, or agent in the course of defending any suit under paragraph 1 of this Article V shall be paid by the corporation in advance of the final disposition of the action, suit or proceeding, upon receipt of an undertaking by or on behalf of the director, officer, employee, or agent to repay such amounts if it is ultimately determined that he is not entitled to be indemnified by the corporation. The corporation shall pay these expenses as they are incurred by the person who may be entitled to indemnification.

**Table of Contents**

3. *Continuation of Right to Indemnification.* The indemnification and advancement of expenses expressly provided by this bylaw shall continue as to a person who has ceased to be a director, officer, employee or agent and shall inure to the benefit of his heirs, executors and administrators.

4. *Intent of Bylaw.* The intent of this Article V is to provide the broadest possible rights to indemnification to the directors, officers, employees, and agents of the corporation permissible under the law of Delaware and not to affect any other right to indemnification that may exist.

CytRx Corporation holds an insurance policy covering directors and officers under which the insurer agrees to pay, with some exclusions, for any claim made against our directors and officers for a wrongful act that they may become legally obligated to pay or for which we are is required to indemnify our directors or officers.

Insofar as indemnification for liabilities arising under the Securities Act of 1933, as amended (the Securities Act ), may be permitted for directors, officers and controlling persons of the Company under the above provisions, or otherwise, the Commission has advised us that, in its opinion, such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Company of expenses incurred or paid by a director, officer or controlling person of the Company in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Company will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

**ITEM 16. EXHIBITS**

The following exhibits are filed herewith or incorporated by reference as a part of this Registration Statement:

- 4.1 Certificate of Amendment to Restated Certificate of Incorporation (incorporated herein by reference to the Company's proxy statement filed on June 7, 2005)
- 4.2 Certificate of Amendment to Restated Certificate of Incorporation (incorporated herein by reference to the Company's proxy statement filed on June 10, 2002)
- 4.3 Certificate of Amendment to Restated Certificate of Incorporation (incorporated herein by reference to the Company's current report on Form 8-K filed on September 12, 2000)
- 4.4 Restated Certificate of Incorporation (incorporated by reference to the Company's restated registration statement on Form S-3 filed on November 5, 1997, File Number 333-39607)
- 4.5 Bylaws, as amended (incorporated by reference to the Company's registration statement on Form S-8 filed on July 21, 1997, File Number 333-31717)
- 4.6 Shareholder Protection Rights Agreement dated April 16, 1997 between CytRx Corporation and American Stock Transfer & Trust Company as Rights Agent (incorporated herein by reference to the Company's quarterly report on Form 10-Q for the quarter ended March 31, 1997)
- 4.7 Form of Common Stock Purchase Warrant between CytRx Corporation and each of the investors in the March 2006 private placement (incorporated herein by reference to the Company's current report on Form 8-K filed on March 3, 2005)
- 4.8 Securities Purchase Agreement, dated as of March 2, 2006, by and among CytRx Corporation and the Investors named therein (incorporated herein by reference to the Company's current report on Form 8-K filed on March 3, 2005)



Edgar Filing: CYTRX CORP - Form S-3

- 4.9 Registration Rights Agreement, dated as of March 2, 2006, by and among CytRx Corporation and the Investors named therein (incorporated herein by reference to the Company's current report on Form 8-K filed on March 3, 2005)
- 5 Opinion of Troy & Gould Professional Corporation \*
- 23.1 Consent of Troy & Gould Professional Corporation (included in Exhibit 5)

II-4

---

**Table of Contents**

23.2 Consent of BDO Seidman, LLP \*

24 Power of Attorney (included on page II-6).

\* Included  
herewith

**ITEM 17. UNDERTAKINGS**

(a) The undersigned Company hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) To include any prospectus required by section 10(a)(3) of the Securities Act;

(ii) To reflect in the prospectus any facts or events arising after the effective date of this registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in this registration statement; and

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement; provided, however, that (i) and (ii) do not apply if the registration statement is on Form S-3, and the information required to be included in a post-effective amendment is contained in periodic reports filed with or furnished to the Commission by the registrant pursuant to section 13 or section 15(d) of the Exchange Act that are incorporated by reference in the registration statement.

(2) That, for the purpose of determining any liability under the Securities Act, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(b) The undersigned Company hereby undertakes that, for purposes of determining any liability under the Securities Act, each filing of the Company's annual report pursuant to section 13(a) or section 15(d) of the Exchange Act (and, where applicable, each filing of an employee benefit plan's annual report pursuant to section 15(d) of the Exchange Act) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(c) Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the Company pursuant to the foregoing provisions, or otherwise, the Company has been advised that in the opinion of the Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Company of expenses incurred or paid by a director, officer or controlling person of the Company in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Company will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

**Table of Contents****SIGNATURES**

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Registration Statement on Form S-3 to be signed on its behalf by the undersigned, thereunto duly authorized in the City of Los Angeles, State of California, on April 12, 2006.

**CYTRX CORPORATION**

By: /s/ STEVEN A. KRIEGSMAN  
 Steven A. Kriegsman  
 President and Chief Executive Officer

**POWER OF ATTORNEY**

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Steven A. Kriegsman his true and lawful attorney-in-fact and agent, with full power of substitution, for him in any and all capacities, to sign this Registration Statement and any amendments hereto, and to file the same, with exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorney-in-fact and agent full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as he might do or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent, or his substitute or substitutes, may do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed by the following persons in the capacities and on the dates indicated.

<b>Signature</b>	<b>Title</b>	<b>Date</b>
/s/ STEVEN A. KRIEGSMAN  Steven A. Kriegsman	President and Chief Executive Officer and Director	April 12, 2006
/s/ MATTHEW NATALIZIO  Matthew Natalizio	Chief Financial Officer and Treasurer (principal financial and accounting officer)	April 12, 2006
/s/ LOUIS J. IGNARRO  Louis J. Ignarro, Ph.D	Director	April 12, 2006
/s/ MAX LINK  Max Link	Director	April 12, 2006
/s/ JOSEPH RUBINFELD  Joseph Rubinfeld, Ph.D	Director	April 12, 2006
/s/ MARVIN R. SELTER  Marvin R. Selter	Director	April 12, 2006

/s/ RICHARD L. WENNEKAMP

Director

April 12, 2006

Richard L. Wennekamp

II-6

---

**Table of Contents**

**EXHIBIT INDEX**

The following exhibits are filed herewith or incorporated by reference as a part of this Registration Statement:

- 4.1 Certificate of Amendment to Restated Certificate of Incorporation (incorporated herein by reference to the Company's proxy statement filed on June 7, 2005)
- 4.2 Certificate of Amendment to Restated Certificate of Incorporation (incorporated herein by reference to the Company's proxy statement filed on June 10, 2002)
- 4.3 Certificate of Amendment to Restated Certificate of Incorporation (incorporated herein by reference to the Company's current report on Form 8-K filed on September 12, 2000)
- 4.4 Restated Certificate of Incorporation (incorporated by reference to the Company's restated registration statement on Form S-3 filed on November 5, 1997, File Number 333-39607)
- 4.5 Bylaws, as amended (incorporated by reference to the Company's registration statement on Form S-8 filed on July 21, 1997, File Number 333-31717)
- 4.6 Shareholder Protection Rights Agreement dated April 16, 1997 between CytRx Corporation and American Stock Transfer & Trust Company as Rights Agent (incorporated herein by reference to the Company's quarterly report on Form 10-Q for the quarter ended March 31, 1997)
- 4.7 Form of Common Stock Purchase Warrant between CytRx Corporation and each of the investors in the March 2006 private placement (incorporated herein by reference to the Company's current report on Form 8-K filed on March 3, 2005)
- 4.8 Securities Purchase Agreement, dated as of March 2, 2006, by and among CytRx Corporation and the Investors named therein (incorporated herein by reference to the Company's current report on Form 8-K filed on March 3, 2005)
- 4.9 Registration Rights Agreement, dated as of March 2, 2006, by and among CytRx Corporation and the Investors named therein (incorporated herein by reference to the Company's current report on Form 8-K filed on March 3, 2005)
- 5 Opinion of Troy & Gould Professional Corporation \*
- 23.1 Consent of Troy & Gould Professional Corporation (included in Exhibit 5)
- 23.2 Consent of BDO Seidman, LLP \*
- 24 Power of Attorney (included on page II-6).

\* Included  
herewith