CYTRX CORP
Form S-1/A
April 08, 2005

As filed with the Securities and Exchange Commission on April 8, 2005

Reg. No. 333-122732

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Amendment No. 1 on Form S-3
to
FORM S-1

REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

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

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

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

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

With a copy to:
Sanford J. Hillsberg, Esq.
Istvan Benko, 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. o

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. þ

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. o

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 delivery of the prospectus is expected to be made pursuant to Rule 434, please check the following box. o

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.

Information contained in this prospectus is subject to completion or amendment. A registration statement relating to these securities has been filed with the Securities and Exchange Commission. These securities may not be sold until the registration statement becomes effective. This prospectus is not an offer to sell and is not a solicitation of an offer to buy these securities in any state in which an offer, solicitation or sale is not permitted.

SUBJECT TO COMPLETION, APRIL 8, 2005

PROSPECTUS

CYTRX CORPORATION

27,243,613 Shares

Common Stock

All of the shares of our common stock offered hereby are being sold by the securityholders listed in this prospectus. See Selling Securityholders. Each of the shares of our common stock is accompanied by one share of our Series A junior participating preferred stock purchase rights that trades with our common stock. Of the shares offered, 17,334,494 shares are owned by some of the selling securityholders as of the date of this prospectus and 9,909,119 shares are issuable upon the exercise of outstanding warrants to purchase our common stock held by the selling securityholders. The number of shares offered by the selling securityholders is subject to increase in certain events by reason of so-called antidilution provisions contained in the warrants held by them. 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. See Use of Proceeds.

Our common stock is traded on the Nasdaq SmallCap Market under the symbol CYTR . On April 7, 2005, the last sale price for the common stock as reported on the Nasdaq SmallCap Market was $1.28**.**

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. See Plan of Distribution. 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.

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 _____, 2005

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.

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THE COMPANY

General

CytRx Corporation is a biopharmaceutical research and development company, based in Los Angeles, California, with an operating obesity and type 2 diabetes subsidiary 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. RNAi is a new technology for silencing genes in living cells and organisms. Our small molecule therapeutics efforts include our clinical development of three, oral drug candidates that we acquired in October 2004, as well as our drug discovery operations conducted in the laboratory of our subsidiary. In addition to our work in small molecule therapeutics and RNAi, we are involved in the development of a DNA-based HIV vaccine and have entered into strategic alliances with respect to the development of several other products using our other technologies.

Since our incorporation in Delaware in 1985, we have been engaged in the development of pharmaceutical products. July 2002, the time of our merger with Global Genomics Capital, Inc., or Global Genomics, marked a change in the focus of our company. Subsequent to the Global Genomics merger, we modified our corporate business strategy by discontinuing any further research and development efforts for our pre-merger pharmaceutical technologies and began to seek strategic relationships with other pharmaceutical companies to complete the development of those technologies. Instead of continuing research and development for those technologies, we focused our efforts on acquiring 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 the University of Massachusetts Medical School, or UMMS, covering potential applications for the medical school s proprietary RNAi technology in the treatment of specified diseases, including those within the areas of obesity and

type 2 diabetes; amyotrophic lateral sclerosis, or ALS, commonly referred to as Lou Gehrig s disease, which is a progressive neurodegenerative disease that results in motor neuron degeneration of the brain and spinal cord and eventual paralysis; and human cytomegalovirus, or CMV, which is a herpes virus that often affects HIV patients. At that time, we also acquired an exclusive license from UMMS covering the medical school s proprietary technology with potential gene therapy applications within the area of cancer. In May 2003, we broadened our strategic alliance with UMMS by acquiring an exclusive license from that institution 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 the next three years 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.

As part of our strategic alliance with UMMS, we agreed to fund certain discovery and pre-clinical research at the medical school relating to the use of our technologies, licensed from UMMS, for the development of therapeutic products within certain fields. To date, we have entered into agreements with UMMS to sponsor research in the areas of obesity and type 2 diabetes, ALS and CMV retinitis. In addition, we have entered into an agreement with Massachusetts General Hospital to sponsor research at that institution that will utilize our proprietary gene silencing technology in the area of ALS.

In conjunction with our work with UMMS, in September 2003, we purchased 95% of CytRx Laboratories, Inc. (formerly known as Araios, Inc.), our research and development subsidiary, which had been recently formed to develop small molecule and RNAi-based therapeutics for the prevention, treatment and cure of obesity and type 2 diabetes. This subsidiary is focusing on using genomic and proteomic based drug discovery technologies combined with our proprietary gene silencing technology to accelerate the process of screening and identifying potential drug targets and pathways for these diseases. Through this subsidiary, we are seeking to develop orally active drugs against promising targets and pathways relevant to obesity and type 2 diabetes.

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 with broad therapeutic applications in neurology, diabetes and cardiology. The acquired assets include three oral, clinical stage drug candidates and a library of 500 small molecule drug candidates. The acquisition positions us as a clinical-stage company, as we expect to initiate a Phase II trial for ALS with one of our new compounds, arimoclomol, in the second quarter of 2005.

Although we intend to internally fund or carry out the research and development related to the drug candidates that we acquired from Biorex, and, through our obesity and type 2 diabetes subsidiary, the early stage development work for certain product applications based on the RNAi and other technologies that we licensed from UMMS, we may also seek to secure strategic alliances or license agreements with larger pharmaceutical 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.

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, which was recently formed, 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 pappiloma 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 Genomics, Inc., or Blizzard, and Psynomics Inc. 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-inducers

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 a way to deal with these potentially toxic mis-folded proteins. Molecular chaperone proteins 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 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 transgenic mice that express the human mutated SOD1 gene that causes certain cases of ALS, 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 disease can be slowed, halted or reversed and affected cells can be restored to full functionality. In *in vitro* studies, mammalian cells engineered to over-express molecular chaperones have increased cross-protection against a variety of otherwise lethal and toxic stresses. In *in vivo* studies, transgenic mice engineered to over-express a molecular chaperone had improved myocardial function, preserved metabolic function and reduced infarct size after ischemia/reperfusion. Increased molecular chaperone expression also significantly increased the lifespan in a mouse model for spinal and bulbar muscular atrophy, a motor neuron disease. We believe that these studies give substantial support within the scientific community for new drugs that are capable of activating a cytoprotective stress response.

Among the assets recently 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 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 the drug candidates acquired from Biorex 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 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 the literature 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 Technology

RNAi technology is a recently discovered technology that 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 *in vitro* and *in vivo* to target specific mRNAs, thus reducing the levels of the specific protein product coded for by that gene 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 for classical, orally-available small molecule drugs and for direct therapeutic applications when technically feasible. As a drug discovery tool, we intend to use RNAi to identify and validate novel targets, which could then be used to discover small molecule therapeutics for the treatment and prevention of obesity and type 2 diabetes. As a therapeutic, we are conducting pre-clinical efficacy studies to determine whether to proceed with human clinical trials using RNAi to silence specific genes that cause 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 will act in an advisory capacity to help us develop therapeutics for specific diseases.

In mammals and human cells, gene silencing can be triggered by delivering dsRNA molecules directly into 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 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 two clinical trials using RNAi, namely safety trials for age-related macular degeneration by Acuity Pharmaceuticals and Sirna Therapeutics.

Product Development

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 with potential therapeutic applications in certain defined areas that include obesity, type 2 diabetes, ALS and CMV, as well as a DNA-based HIV vaccine technology and a cancer therapeutic technology. In addition, we have entered into a collaboration and invention disclosure agreement with UMMS under which UMMS will disclose to us certain new technologies developed at UMMS over the next

three years 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.

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, have received a $16 million grant from the NIH. This grant is currently funding a Phase I clinical trial of a vaccine candidate using our licensed technology. The investigational new drug application, or IND, for that trial was filed in January 2004 and allowed by the FDA to go into effect in March 2004. Enrollment of volunteers for this trial began in April 2004, and we anticipate completing this trial in the first half of 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, which is being conducted by UMMS and ABL. 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.

Finally, we have also licensed a cancer treatment technology from UMMS that is based on a naked DNA approach in which the DNA material will be delivered by direct injection into the tumor or other localized administration.

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 $1.3 million for 2005 and approximately $737,000 for 2006. Our license agreements with UMMS require us to make payments of an aggregate of up to $105,000 per year to maintain all of our licenses, with such aggregate annual payments increasing to as much as $145,000 if we are not then conducting certain sponsored research at the institution. 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 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, cancer 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 $750,000 in 2005 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 diabetes in the United States. Scientists at UMMS, as part of our strategic alliance, are researching, with funding that we have provided, the specific genetic relationship of type 2 diabetes to obesity. The research is 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 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 gene silencing technology.

In addition, one of the drug candidates acquired from Biorex, iroxanadine, 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 2006.

Although we initially intend to develop arimoclomol, another of the drug candidates acquired from Biorex, 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 2006, as arimoclomol has already been tested in two Phase I clinical trials.

Research and Development Subsidiary

In addition to the obesity and diabetes work being done under our sponsored research agreement with UMMS, in September 2003, we purchased 95% of CytRx Laboratories, Inc. (formerly known as Araios, Inc.), our research and development subsidiary, which had been recently formed by Dr. Michael P. Czech to develop orally active small molecule and RNAi-based drugs for the prevention, treatment and cure 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, treat and cure 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 subsidiary will focus on using a structure based drug discovery approach to accelerate the process of screening and identifying potential drug targets and pathways for these diseases. Through our subsidiary, we will seek to develop orally administered drugs that are based on promising targets and pathways that we may be able to identify.

Dr. Czech is a prominent scientist in the fields of obesity and type 2 diabetes at UMMS, is a member of our Scientific Advisory Board, heads our subsidiary s Scientific Advisory Board and holds a 5% equity interest in the subsidiary. We provided the subsidiary in September 2003 with initial capital of approximately $7,000,000 to fund the staffing of its operations with managerial and scientific personnel and its initial drug development activities.

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 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.

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.

Our drug candidate, arimoclomol, acquired from Biorex in October 2004, was previously shown to be well tolerated in two Phase I clinical trials in healthy volunteers. Based on this, and results indicating efficacy of the drug candidate in animal models of neuronal damage, including the published efficacy data of the drug in animal models

of ALS, we expect to begin a Phase II clinical trial with arimoclomol for the treatment of ALS in the second quarter of 2005. We are scheduled to discuss the proposed Phase II clinical trial with the FDA in the coming weeks.

In October 2003, we entered into sponsored research agreements with UMMS and Massachusetts General Hospital, pursuant to which we will sponsor certain ALS research at those institutions utilizing our proprietary 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. We have funded approximately $302,000 of research under that agreement during its first year, and have committed to fund approximately $280,000 of research under that agreement during its second year and approximately $288,000 of research under that agreement during the third year of the program.

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 agreed to fund approximately $487,000 of sponsored research at Massachusetts General Hospital through the end of 2005. In March 2004, Dr. Brown joined our Scientific Advisory Board and entered into a consulting agreement with us.

Cardiovascular Disease

Preclinical results by third parties with our drug candidate, iroxanadine, indicate that it has therapeutic potential for the treatment of cardiovascular atherosclerosis. If iroxanadine 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.

Pre-Global Genomics Merger Technologies

Therapeutic Copolymer Program

Prior to the merger with Global Genomics, 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 93%, 81% and 94% of our total revenues for 2004, 2003 and 2002, 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-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 April 2004, we received an additional $100,000 milestone fee 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.

2002 Merger with Global Genomics

On July 19, 2002, we completed the acquisition of Global Genomics. The acquisition of Global Genomics was accomplished through a merger of our wholly-owned subsidiary, GGC Merger Corporation, with and into Global Genomics. Global Genomics was the surviving corporation in the merger with GGC Merger Corporation and is now our wholly-owned subsidiary. We have changed Global Genomics name to GGC Pharmaceuticals, Inc., but for purposes of this prospectus, we will continue to refer to the company as Global Genomics. For accounting purposes, we were deemed the acquiror of Global Genomics.

In the Global Genomics merger, each outstanding share of common stock of Global Genomics was converted into 0.765967 shares of our common stock. Accordingly, a total of 8,948,204 shares of our common stock, or approximately 41.7% of our common stock outstanding immediately after the merger, were issued to the common stockholders of Global Genomics, and an additional 1,014,677 shares of our common stock were reserved for issuance upon the exercise of the outstanding Global Genomics warrants that we assumed in the merger. Other than the foregoing stock, we paid no other consideration to the Global Genomics shareholders.

At the time of the Global Genomics merger, there were no material relationships between Global Genomics or any of its shareholders or affiliates and us, except that on July 16, 2002, Global Genomics three designees to our board of directors, Steven A. Kriegsman, Louis J. Ignarro, Ph.D. and Joseph Rubinfeld, Ph.D., were elected directors and Mr. Kriegsman became our Chief Executive Officer. Mr. Kriegsman was Global Genomics Chairman and Dr. Ignarro was a director of Global Genomics at that time. On the date of the merger, the controlling shareholder of Global Genomics was Mr. Kriegsman, who beneficially owned, on a fully diluted basis, approximately 40.4% of Global Genomics equity interests.

Genomics Investments

In connection with our merger with Global Genomics, 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 was in the process of returning its licensed intellectual property to the University of Minnesota.

Employees

As of December 31, 2004, we had 23 full-time employees, 14 of whom were engaged in research and development activities and nine of whom were involved in management and administrative operations. All of the employees engaged in research and development activities hold Ph.D. degrees, and one also holds an M.D. degree.

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 related to the early stage of our diabetes, obesity, 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, uncertainties regarding the scope of the clinical testing that may be required by regulatory authorities for the drug candidates acquired from Biorex Research and Development Company, RT, or Biorex, and other products and the outcomes of those tests, the significant time and expense that will be incurred in developing any of the potential commercial applications for our small molecules or RNAi technology, our need for additional capital to fund our ongoing working capital needs, including ongoing research and development expenses related to the drug candidates purchased from Biorex, risks relating to the enforceability of any patents covering our products and to the possible infringement of third party patents by those products, and the impact

of third party reimbursement policies on the use of and pricing for our 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.

RISK FACTORS

You should carefully consider the following risks before deciding to purchase shares of our common stock. If any of the following risks actually occur, the trading price of our common stock could decline, and you could lose all or part of your investment. 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 $16.4 million, $17.8 million and $6.2 million for the years ended December 31, 2004, 2003 and 2002, respectively, and we had an accumulated deficit of approximately $106.2 million as of December 31, 2004. 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. Unless we are able to acquire products from third parties that are already being marketed and that can be profitably marketed by us, we anticipate it will take a minimum of three years (and possibly longer) for us to generate recurring revenues, since we expect that it will take at least that long before the development of any of our licensed or other current potential products is completed, marketing approvals are obtained from the United States Food and Drug Administration, or FDA, and commercial sales of any of these products can begin.

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

Our revenues were $428,000, $94,000 and $1.1 million during the years ended December 31, 2004, 2003 and 2002, respectively. We will not have significant recurring operating revenues until at least one of the following occurs:

- We are able to complete the development of and commercialize one or more of the products that we are currently developing, which may require us to first enter into license or other arrangements with third parties.
- One or more of our currently licensed products is commercialized by our licensees, thereby generating royalty income for us.
- We are able to acquire products from third parties that are already being marketed or are approved for marketing.

We are likely to incur negative cash flow from operations until such time, if ever, as we can generate significant recurring revenues. On January 26, 2005, we completed a private placement financing and received net proceeds of approximately $19.5 million. Although we believe that we have adequate financial resources to support our currently planned level of operations into the second quarter of 2006, it is likely that we will be dependent on obtaining financing from third parties to continue to meet our obligations to UMMS, and maintain our operations, including our planned levels of operations for our obesity and type 2 diabetes subsidiary and our ongoing research and development efforts related to the drug candidates acquired from Biorex. We have no commitments from third parties to provide us with any additional debt or equity financing. Accordingly, future financing may be unavailable to us or only available on terms that substantially dilute our existing stockholders. A lack of needed financing could force us to reduce the scope of, or terminate, our operations, or to seek a merger with or be acquired by another company. There can be no assurance that we would be able to identify an appropriate company to merge with or be acquired by or that we could consummate such a transaction 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 have represented 93%, 81% and 94% of our total revenues for the years ended December 31, 2004, 2003 and 2002, respectively. We have already licensed most of the potential applications for this technology, and there can be no assurance that we will be able to generate additional license fee revenues from any new licensees for 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. However, Vical has only recently commenced two Phase I clinical trials of products utilizing TranzFect as a component of a vaccine to prevent CMV. 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.

We Have Changed Our Business Strategy, Which Will Require Us, in Certain Cases, to Find and Rely Upon Third Parties for the Development of Our Products and to Provide Us With Products

Following our merger with Global Genomics, we modified our business strategy of internally developing Flocor and the other, then-current, potential products that we had not yet licensed to third parties. Instead, we began to seek to enter into strategic alliances, license agreements or other collaborative arrangements with other pharmaceutical companies that would provide for those companies to be responsible for the development and marketing of those products. In June 2004, we licensed Flocor, the primary potential product that we held prior to the Global Genomics merger and which we had not already licensed to a third party, to SynthRx, Inc., a recently formed Houston, Texas-based biopharmaceutical company, under a strategic alliance that we entered into with that company in October 2003. Although we intend to internally fund or carry out a significant portion of the research and development related to at least one of the drug candidates that we acquired from Biorex, and, through our subsidiary, the early stage development work for certain product applications based on the RNAi and other technologies that we licensed from UMMS, and we may seek to fund all of the later stage development work for our potential ALS products, the completion of the development, manufacture and marketing of these products is likely to require, in many cases, that we enter into strategic alliances, license agreements or other collaborative arrangements with larger pharmaceutical companies for this purpose.

There can be no assurance that our products will have sufficient potential commercial value to enable us to secure strategic alliances, license agreements or other collaborative arrangements with suitable companies on attractive terms or at all. If we are unable to enter into collaborative agreements, we may not have the financial or other resources to continue development of a particular product or the development of any of our products. In connection with the Phase I clinical trial currently being conducted by UMMS and ABL on an HIV vaccine candidate that utilizes a technology that we licensed from UMMS, we do not have a commercial relationship with the company that provided an adjuvant for the vaccine for the trial. If we are not able to enter into an agreement with this company on terms favorable to us or at all, 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 these 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 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 will 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 the institution relating to the development of therapeutic products based on the UMMS proprietary 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 $2.4 million for 2005, approximately $1.5 million for 2006 and approximately $310,000 for 2007. We have also agreed to fund approximately $209,000 of sponsored research at Massachusetts General Hospital during 2005 and 2006. 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, cancer and an HIV vaccine, under our licenses, those milestone payments could aggregate up to $16.1 million. 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 were to successfully develop any of those products, 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.

Although we believe that an existing grant from the National Institute of Health, or NIH, will be sufficient to fund substantially all of the costs of an ongoing Phase I trial of the HIV vaccine candidate using the technology we licensed from UMMS and Advanced BioScience Laboratories, or ABL, we could be required to fund substantial expenses of the trial not covered by the grant. Under our license for this technology, 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. We do not have any NIH or other governmental funding for these future trials, and there can be no assurance that we will be able to secure such funding for any of these trials.

The expenditures potentially required under our agreements with UMMS and ABL, together with the operating capital requirements of our obesity and type 2 diabetes subsidiary, our planned sponsored research funding for Massachusetts General Hospital and our development of the drug candidates acquired from Biorex, substantially exceed our current financial resources. Although we raised approximately $19.5 million in January 2005, net of transaction expenses, those required expenditures will nonetheless require us to raise additional capital or to secure a licensee or strategic partner to fulfill our obligations to UMMS and to develop any products based on the technologies that we have licensed from UMMS or any products that we acquired from Biorex, and to continue the operations of our subsidiary at the currently contemplated level. If we are unable to meet our various financial obligations under license agreements with UMMS, we could lose all of our rights under those agreements. If we were to have inadequate financial resources at that time, we also could be forced to reduce the level of, or discontinue, operations at our subsidiary.

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 are at various stages of development and 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 and we may not have the financial resources to continue to develop our products and may have to terminate our operations.

The Approach We Are Taking to Discover and Develop Novel Drugs Using RNAi and Other Technologies is Unproven and May Never Lead to Marketable Products

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

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, iroxanadine and bimoclomol), and a library of small molecule drug candidates. Although each of arimoclomol, iroxanadine 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, iroxanadine 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.

We expect to initiate Phase II clinical testing for arimoclomol for ALS in the second quarter of 2005, however there are no assurances that the clinical testing will be successful. We believe that the FDA may accept the completion of a successful Phase II clinical trial as sufficient to enable us to submit a New Drug Application, or NDA, however there are no guarantees that the FDA will accept our Phase II study 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 beyond our estimated costs. 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 would show any efficacy for any other indications.

Iroxanadine has been tested in two Phase I clinical trials and one Phase II clinical trial which showed 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 iroxanadine will show any efficacy in the intended uses we are seeking. We may also attempt to license iroxanadine to larger pharmaceutical or biotechnology companies for cardiovascular indications; however, there is no guarantee that any such company will be interested in licensing iroxanadine from us or on terms that are favorable 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. 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 Subsidiary May Not Be Able to Develop Products

In order to develop new obesity and type 2 diabetes products, our subsidiary, CytRx Laboratories, will first need to identify appropriate drug targets and pathways. We will be 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 highly 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 that are available for this purpose. We currently plan to seek a strategic alliance with a major pharmaceutical or biotechnology company at a relatively early stage in our development work to complete the development, clinical testing and manufacturing and marketing of our obesity and type 2 diabetes products, 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 the Scientific Advisory Board of our subsidiary, Dr. Jack Barber, our Senior Vice President Drug Development, and Dr. Mark A. Tepper, the President of our subsidiary and a Vice President of CytRx Corporation, in establishing the scientific goals and strategies of our subsidiary.

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 those studies will 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 Unlikely to Recover Any Amounts from Global Genomics Portfolio Companies

Due to its inability to raise needed capital, Blizzard, which was Global Genomics principal portfolio company, has been unable to complete the development of any of its products and has been notified by the licensor of its core technologies that it is in default under its license for those technologies. Global Genomics other portfolio company is at a very early stage, is operating without any full-time or salaried employees and has not been able to raise the capital it will need to fund its planned operations and to acquire licenses to certain technologies that it will require. Accordingly, it appears unlikely that either of Global Genomics portfolio companies will generate revenues for us in the future and, in 2003, we recorded a write-off of the carrying value of our investments in those companies.

We May Be Involved in Legal Proceedings That Could Affect Our Business Operations or Financial Condition

We may be involved, from time to time, in investigations and proceedings by governmental or self-regulatory agencies, certain of which could result in adverse judgments, fines or other sanctions. In February 2004, we were notified by the Massachusetts State Ethics Commission, or the Massachusetts Commission, that it had initiated a preliminary inquiry into whether our previous retention of a consultant who introduced us to UMMS constituted an improper conflict of interest under Massachusetts ethics laws. UMMS has recently advised us that it continues to believe that its agreements with us provided excellent value for UMMS, that it anticipates that the Massachusetts Commission s review of the terms of those agreements will confirm that the agreements were fair to UMMS, and that it believes that the Massachusetts Commission will concur with the resolution of the conflict proposed by UMMS under which the consultant will forfeit to UMMS certain of the compensation that the consultant was to receive from us.

We Are Subject to Intense Competition That Could Materially Impact Our Operating Results

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.

Obtain FDA and other regulatory approvals for their products before 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 or 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, Inc., Alnylam Pharmaceuticals, Inc., Benitec Ltd., Nucleonics, Inc. 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® by Glaxo SmithKline PLC, Actos® by Eli Lilly & Co., Glucophage® by Bristol-Myers Squibb Co., Symlin® by Amylin Pharmaceuticals, Inc. and Starlix® by Novartis and the obesity drugs Xenical® by F. Hoffman-La Roche Ltd. and Meridia® 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., Epimmune, Inc., AlphaVax, Inc. and Immunitor Corporation.

Currently, Rilutek®, 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 and Oxford BioMedica plc, which may be seeking to develop an RNAi-based therapy for ALS. 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, Guilford Pharmaceuticals, Phytopharm plc, Cephalon, Inc. and Ceregene, Inc.

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, even though Flocor acts by a different mechanism to prevent damage due to blood coagulation. In the sickle cell disease area, Flocor would compete against companies that are developing or marketing other products to treat sickle cell disease, such as Droxia® (hydroxyurea) marketed by Bristol-Myers Squibb Co. and Dacogen , 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 marketed by Antigenics, Inc. and adjuvants marketed by Corixa Corp. Blizzard s products, if ever developed, will compete with a number of currently marketed products, including those offered by Axon Instruments, Inc., Affymetrix, Inc., Applied Precision, LLC, Perkin Elmer, Inc. and Agilent Technologies, Inc.

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. Accordingly, we will be dependent upon contract manufacturers or our strategic alliance partners

to manufacture these supplies, or we will need to acquire the ability to manufacture these supplies ourselves, which could be very difficult, time-consuming and costly. We do not have manufacturing supply arrangements for our products, including any of the licensed RNAi technology, the drug candidates acquired from Biorex or, with the exception of the clinical supplies for the current Phase I trial, 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, or acquire the ability to manufacture the products

ourselves, on attractive terms or at all. Delays in, or a failure to, secure these arrangements or abilities 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. 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 the 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 will withstand third-party 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 use of our products in human clinical trials or the commercial marketing of these products. We are in the process of obtaining clinical trial insurance for our planned clinical trial of arimoclomol for the treatment of ALS and will seek to obtain such insurance for any other clinical trials that we conduct, as well as liability insurance for any products that we market, although there can

be no assurance that we will be able to obtain such insurance in the amounts we are seeking 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, if someone asserts a claim against us and our insurance or the insurance coverage of our licensees or if their other financial resources are inadequate to cover a successful claim, such successful claim could have a material adverse effect on our financial condition or cause us to discontinue operations. 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.

We May Be Delisted from the Nasdaq SmallCap Market if Our Future Filings Are Not Timely

In May 2004, a Nasdaq Listing Qualifications Panel ruled that our common stock would remain listed on the Nasdaq SmallCap Market, notwithstanding the fact that we filed our Annual Report on Form 10-K for the year ended December 31, 2003 with the SEC after the deadline for its filing. In addition, that Panel also ruled that our common stock would be delisted if we failed to timely file any reports with the SEC required for any period ending on or before June 30, 2005, and that we would not be entitled to a hearing before a Nasdaq Listing Qualifications Panel with respect to any finding by Nasdaq s staff of such a filing deficiency. Our inability to receive a hearing would make it extremely difficult, if not impossible, to cure any late filing deficiency. If we fail to comply with this condition for continued listing and our common stock is delisted from the Nasdaq Small Cap Market, we may seek to list our common stock for trading on the American Stock Exchange or a regional stock exchange or to facilitate trading of our common stock in the over-the-counter market. If our common stock is delisted from the Nasdaq SmallCap Market, however, there is no assurance that our common stock will be listed for trading elsewhere, and an active trading market for our common stock may cease to exist and the delisting could materially and adversely impact the market value of our common stock.

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

We have a stockholder rights plan and provisions in our bylaws that 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 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, 2004, there were outstanding stock options and warrants to purchase approximately 14.5 million shares of our common stock at exercise prices ranging from $0.01 to $2.94 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 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 April 2004, we became temporarily ineligible to continue to use Form S-3 for both of these registrations, so that the holders of these shares could no longer sell their shares under these registrations. Our ineligibility to register resales on Form S-3 may have created liability under certain of our registration rights agreements if we are not deemed to have amended certain existing registrations in a reasonable period of time so as to permit the holders to again be able to sell their shares under those registrations. We are in the process of reinstating the registrations so as to permit the holders to again be able to sell their shares under these registrations. 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 filed with the SEC a registration statement covering 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. 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 2005 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, performance-based awards, share appreciation rights, and employee share purchase plans. We will have to apply the new financial accounting rules beginning in the third quarter of 2005. 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. These compensation expenses may be larger than the compensation expense that we would be required to record were we able to compensate these persons with cash in lieu of securities. 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.