CYTRX CORP
Form 10-K/A
May 22, 2006

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UNITED STATES SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549
Form 10-K/A
Amendment No. 1

(Mark One)

þ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2005

or

o **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF SECURITIES EXCHANGE ACT OF 1934**

Commission File No. 0-15327

CytRx Corporation

(Exact name of Registrant as specified in its charter)

Delaware	**58-1642740**
(State or other jurisdiction of incorporation or organization)	*(I.R.S. Employer Identification No.)*
11726 San Vicente Blvd, Suite 650, Los Angeles, California	**90049**
(Address of principal executive offices)	*(Zip Code)*

Registrant s telephone number, including area code:
(310) 826-5648

Securities registered pursuant to Section 12(b) of the Act:
None
Securities registered pursuant to Section 12(g) of the Act:
Common Stock, $.001 par value per share

Indicate by check mark with the Registrant is a well-known seasoned issuer (as defined in Securities Act Rule 405). Yes o No þ

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934. Yes o No þ

Indicate by check mark whether the Registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months and (2) has been subject to such filing requirements for the past 90 days. Yes þ No o

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of the Registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K þ

Indicate by check mark whether the Registrant is a large accelerated filer, an accelerated filer, or a non-accelerated filer.

Large accelerated filer o Accelerated filer o Non-accelerated filer þ

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 2b-2 of the Act). Yes o No þ

The aggregate market value of the Registrant s common stock held by non-affiliates on June 30, 2005 was approximately $49,272,313. On March 23, 2006, there were 70,457,988 shares of the Registrant s common stock

outstanding, exclusive of treasury shares.

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EXPLANATORY NOTE

CytRx Corporation (the Company) is amending its Annual Report on Form 10-K for the fiscal year ended December 31, 2005. The purpose of this amendment is to restate our consolidated financial statements for the year ended December 31, 2005 and amend the related disclosures in our original Form 10-K, as described below and in Notes 2 and 14 to our Consolidated Financial Statements included in this amendment.

The restatement of our consolidated financial statements is related to the pro forma amounts disclosed in accordance with Statement of Financial Accounting Standards (SFAS) No. 123, *Accounting for Stock-Based Compensation*, which were calculated incorrectly and reported in the stock-based compensation section of our significant accounting policies footnote contained in our original Form 10-K. The restatement also includes a correction in the accounting for antidilution features in certain of our outstanding warrants. On May 20, 2006, the Audit Committee of our Board of Directors approved management s recommendation to restate our consolidated financial statements for the year ended December 31, 2005 to reflect the corrected disclosures in our significant accounting policies footnote and the correction in the accounting for antidilution features in certain of our outstanding warrants.

The following Items and Exhibits of our original Form 10-K are amended by this amendment:

Part II Item 7. Management s Discussion and Analysis of Financial Condition and Results of Operations

Part II Item 8. Financial Statements and Supplementary Data

Part II Item 9A. Controls and Procedures

Part IV Item 15. Exhibits and Financial Statement Schedules

Exhibit 31.1 Certification of Chief Executive Officer

Exhibit 31.2 Certification of Chief Financial Officer

Except for the foregoing Items and Exhibits, this amendment does not modify any disclosures contained in our original Form 10-K. Additionally, this amendment, except for the restatement information, speaks as of the filing date of the original Form 10-K and does not attempt to update the disclosures in our original Form 10-K or to discuss any developments subsequent to the date of the original filing. In accordance with the rules and regulations of the Securities and Exchange Commission, the information contained in the original Form 10-K and this amendment is subject to updated or supplemental information contained in reports filed by us with the Securities and Exchange Commission subsequent to the filing dates of the original Form 10-K and this amendment.

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Exhibit Index located on page 49 of this report.

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SAFE HARBOR STATEMENT UNDER THE PRIVATE SECURITIES LITIGATION REFORM ACT OF 1995

From time to time, we make oral and written statements that may constitute forward-looking statements (rather than historical facts) as defined in the Private Securities Litigation Reform Act of 1995 or by the Securities and Exchange Commission, or SEC, in its rules, regulations and releases, including Section 27A of the Securities Act of 1933, as amended and Section 21E of the Securities Exchange Act of 1934, as amended. We desire to take advantage of the safe harbor provisions in the Private Securities Litigation Reform Act of 1995 for forward-looking statements made from time to time, including, but not limited to, the forward-looking statements made in this Annual Report on Form 10-K, as well as those made in other filings with the SEC.

All statements in this Annual Report, including in Management s Discussion and Analysis of Financial Condition and Results of Operations, 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 documents incorporated by this Annual Report 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 Annual Report, and including risks or uncertainties regarding the scope of the clinical testing that may be required by regulatory authorities for our molecular chaperone co-induction drug candidates, including with respect to arimoclomol for the treatment of amyotrophic lateral sclerosis (ALS or Lou Gehrig s disease), our HIV vaccine candidate and our other product candidates, and the outcomes of those tests; uncertainties related to the early stage of our diabetes, obesity, cytomegalovirus, or CMV, and ALS research; the need for future clinical testing of any small molecules and products based on ribonucleic acid interference, or RNAi, that may be developed by us; the significant time and expense that will be incurred in developing any of the potential commercial applications for our small molecules or RNAi technology; risks or uncertainties related to our ability to obtain capital to fund our ongoing working capital needs, including capital required to fund the RNAi development activities to be conducted by our planned new subsidiary; and risks relating to the enforceability of any patents covering our products and to the possible infringement of third party patents by those products. All forward-looking statements and reasons why results may differ included in this Annual Report 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.

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PART I

Item 1. *Business*

As used in this report, the terms we, our, ours and us refer to CytRx Corporation, a Delaware corporation, unless the context suggests otherwise.

General

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

On October 4, 2004, we acquired all of the clinical and pharmaceutical and related intellectual property assets of Biorex Research & Development, RT, or Biorex, a Hungary-based company focused on the development of novel small molecules based on molecular chaperone co-induction technology, with broad therapeutic applications in neurology, type 2 diabetes, cardiology and diabetic complications. The acquired assets include three oral, clinical stage drug candidates and a library of 500 small molecule drug candidates. We recently entered the clinical stage of drug development with the initiation of a Phase II clinical program with our lead small molecule product candidate arimoclomol for the treatment of amyotrophic lateral sclerosis (ALS or Lou Gehrig s disease). Arimoclomol has received Orphan Drug and Fast Track designation from the U.S. Food and Drug Administration.

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

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

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

In April 2003, we acquired our first new technologies by entering into exclusive license agreements with UMMS covering potential applications for its proprietary RNAi technology in the treatment of specified diseases and in the identification and screening of novel protein targets. In May 2003, we broadened our strategic alliance with UMMS by acquiring an exclusive license from it covering a proprietary DNA-based HIV vaccine technology. In July 2004, we further expanded our strategic alliance with UMMS by

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entering into a collaboration and invention disclosure agreement with UMMS under which UMMS will disclose to us certain new technologies developed at UMMS over a three-year period pertaining to RNAi, diabetes, obesity, neurodegenerative diseases (including ALS) and CMV, and will give us an option, upon making a specified payment, to negotiate an exclusive worldwide license to the disclosed technologies on commercially reasonable terms. Approximately one year remains on the technology disclosure option. As part of our strategic alliance with UMMS, we agreed to fund certain discovery and pre-clinical research at UMMS relating to the use of our technologies, licensed from UMMS, for the development of therapeutic products within certain fields.

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

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

Prior to 2003, our primary technologies consisted of Flocor, an intravenous agent for treatment of sickle cell disease and other acute vaso-occlusive disorders, and TranzFect, a delivery technology for DNA and conventional-based vaccines. In October 2003, we entered into a strategic relationship with another entity to complete the development of Flocor. Our TranzFect technology has been licensed to two companies. We have granted a third party an option to license our TranzFect technology for development as a potential DNA-based prostate cancer adjuvant and may also seek to license this technology as a potential conventional adjuvant for hepatitis C, human 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 and Psynomics. In 2003, we recorded a write-off of our investments in those companies. Our decision to record the write-off was based upon several factors. Those investments, and the write-off of those investments, are further described under Genomics Investments.

Molecular Chaperone Co-Induction Platform

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

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

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

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

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

Among the assets acquired from Biorex were several drug candidates whose mechanism of action is believed to be the co-induction of the stress response, meaning that they do not seem to activate the stress response by themselves, but instead they amplify the production of molecular chaperone proteins that are already activated by disease-induced cellular stress. These drug candidates thus may selectively amplify molecular chaperone proteins specifically in diseased tissue, which would minimize potential drug side-effects. The amplification of this fundamental protective mechanism may have powerful therapeutic and prophylactic potential, with the potential for an extremely broad field of medical therapeutic utility.

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

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

RNAi Platform Technology

RNAi technology 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 useful in laboratory cell culture experiments and in animals (including humans) to target specific mRNAs, thus reducing the levels of the corresponding specific protein product that is coded for by that RNA in the targeted cells. This allows the use of RNAi either as an effective drug discovery tool or potentially as a therapeutic product itself. We intend to develop RNAi technology as both a discovery tool to help identify classical, orally-available small molecule drugs and, potentially through the creation of a new subsidiary, for direct therapeutic applications when technically feasible. As a drug discovery tool, we use RNAi

to identify and validate novel protein targets, which could then be used to discover small molecule therapeutics for the treatment and prevention of diseases such as obesity and type 2 diabetes. As a therapeutic, we are conducting pre-clinical RNAi efficacy studies to determine whether to proceed with human clinical trials using RNAi to silence specific genes that cause certain forms of ALS, CMV retinitis, and type 2 diabetes. In January 2004, Tariq Rana, a scientific authority in delivery and stability of

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RNAi, and in March 2004, Dr. Craig Mello, the co-discoverer of RNAi, each joined our Scientific Advisory Board and they act in an advisory capacity to help us develop RNAi therapeutics for specific diseases. We are currently pursuing a plan, subject to obtaining necessary funding, to transfer all of our RNAi therapeutics assets into a newly-formed subsidiary to accelerate the development and commercialization of drugs based on RNAi technology. In such event, the Company would continue to use its RNAi gene silencing technology as a drug discovery tool to facilitate its small molecule drug discovery program.

In mammals and human cells, gene silencing can be triggered by dsRNA molecules present in the cell s cytoplasm (the region inside the cell membrane but outside the cell nucleus). Specific enzymes (proteins) in the cell called dicer enzymes cut the dsRNA to form small interfering RNA, or siRNA. These siRNA are approximately 21 to 25 nucleotide long pieces of RNA. The siRNA then interact with other cellular proteins to form the RNA-induced silencing complex, or RISC, which causes the unwinding of the bound siRNA. This unwound strand of the siRNA can then act as a template to seek out and bind with the complementary target mRNA, which carries the coding, or instructions, from the cell nucleus DNA. These instructions determine which proteins the cell will produce. When the siRNA-loaded RISC binds with the corresponding mRNA, that message is degraded and the cell does not produce the specific protein that it encodes. Since the siRNA can be designed to specifically interact with a single gene through its mRNA, it can prevent the creation of a specific protein without affecting other genes.

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

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

Product Development

ALS

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

We recently entered the clinical stage of drug development in ALS with the initiation of a Phase II clinical program with our lead small molecule product candidate arimoclomol for the treatment of ALS. Arimoclomol has received Orphan Drug and Fast Track designation from the U.S. Food and Drug Administration. The initial portion of the Phase II clinical program was initiated in September 2005. We expect enrollment in this Phase IIa trial to be complete shortly, and expect to announce results in the third quarter of 2006.

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

Dr. Zuoshang Xu, an Associate Professor of Biochemistry and Molecular Pharmacology at UMMS, is the principal investigator under our sponsored research agreement with UMMS, through which we have agreed to fund approximately $870,000 of research related to the development of an RNAi therapeutic targeting the mutant form of SOD1 that causes certain forms of ALS, of which $654,000 had been paid as of December 31, 2005. We anticipate

that the development of this program will be continued by our planned RNAi subsidiary.

Dr. Robert B. Brown, Jr., a Professor of Neurology at Harvard Medical School, Founder and Director of the Cecil B. Day Laboratory for Neuromuscular Research and a co-discoverer of the mutant SOD1 gene as a cause for certain ALS cases, is the

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principal investigator under our sponsored research agreement with Massachusetts General Hospital. Under the agreement, we have funded approximately $556,000 of sponsored research at Massachusetts General Hospital to increase our basic understanding of certain aspects of the ALS disease process. In March 2004, Dr. Brown joined our Scientific Advisory Board and entered into a consulting agreement with us.

University of Massachusetts Medical School

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

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

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

technologies.

Obesity and Type 2 Diabetes

Obesity and type 2 diabetes are significant health problems. The World Health Organization estimates that, on a worldwide basis, there are more than 300 million cases of obesity and 159 million cases of type 2 diabetes. According to the American Obesity Association, there are currently more than 60 million cases of obesity in the United States, and the American Diabetes Association reports that there are more than 16 million cases of type 2 diabetes in the United States. Scientists in our Worcester laboratory and scientists at UMMS, as part of our strategic alliance, are focused on using cultured adipocytes (fat cells) as a model system for

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

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

In addition, one of the drug candidates acquired from Biorex, 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 2007.

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

Research and Development Laboratory

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

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

Cardiovascular Disease

Preclinical results by third parties with our drug candidate, 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

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

Therapeutic Copolymer Program

Before the Global Genomics merger, our primary focus was on CRL-5861 (purified poloxamer 188), which we also call Flocor. Flocor is an intravenous agent for the treatment of sickle cell disease and other acute vaso-occlusive disorders. Sickle cell disease is an

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

Vaccine Enhancement and Gene Therapy

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

Merck License

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

Vical License

In December 2001, we entered into a license agreement with Vical Incorporated granting Vical exclusive, worldwide rights to use or sublicense our TranzFect poloxamer technology to enhance viral or non-viral delivery of polynucleotides, such as DNA and RNA, in all preventive and therapeutic human and animal health applications, except for (1) the four targets previously licensed by us to Merck, (2) DNA vaccines or therapeutics based on prostate-specific membrane antigen, or PSMA, and (3) sale of a non-regulated product for use as a non-clinical research reagent to increase transfection *in vitro* or in laboratory animals. In addition, the Vical license permits Vical to use TranzFect poloxamer technology to enhance the delivery of proteins in prime-boost vaccine applications that involve the use of polynucleotides (short segments of DNA or RNA). Under the Vical license, we received a non-refundable up-front payment of $3,750,000, and, in addition to annual maintenance payments, we have the potential to receive milestone and royalty payments in the future based on criteria described in the agreement. In each of April 2004 and January 2005, we received additional $100,000 milestone fees related to the commencement of Vical s first FDA Phase I clinical trial for a product incorporating our TranzFect technology. All amounts paid to us by Vical are non-refundable upon termination of the agreement and require no additional effort on our part.

Genomics Investments

In connection with our merger with Global Genomics in July 2002, we acquired indirectly equity interests in two development-stage genomics companies, a 40% equity interest in Blizzard and a 5% equity interest in Psynomics. In

the fourth quarter of 2003, we decided that we would cease funding our investments in those genomics companies to focus on our core strategy of developing human therapeutics for large market indications. In May 2004, we determined that a write-off of those investments in the third quarter of 2003 should have been made. Our decision to record the write-off was based upon several factors, including Blizzard s lack of success

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in raising a significant amount of the financing necessary for it to pursue the commercialization strategy for its products, current financial projections prepared by Blizzard, application of a discounted cash flow valuation model of Blizzard s projected cash flows and the consideration of other qualitative factors. Based upon the quantitative and qualitative factors described above, in addition to others, we determined that the investment in Blizzard had no remaining value as of September 30, 2003 and that a write-off of this investment should have been made in the third quarter of 2003. It is our understanding that, by the end of 2003, Blizzard had ceased operations and, in 2004, returned its licensed intellectual property to the Minnesota Research Fund.

Research and Development Expenditures

Expenditures for research and development activities were $9.1 million, $9.0 million and $4.4 million during the years ended December 31, 2005, 2004 and 2003, respectively. Included in research and development expenses for 2004 was $3.0 million of in-process research and development that was written off in conjunction with our acquisition of assets from Biorex.

Manufacturing

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

Patents and Proprietary Technology

We actively seek patent protection for our technologies, processes, uses, and ongoing improvements and consider our patents and other intellectual property to be critical to our business. We have filed applications for a number of patents and have been granted patents related to technologies, primarily TranzFect and Flocor, we were developing prior to our 2002 merger with Global Genomics. Subsequent to the merger, we acquired patents in connection with our acquisition of intellectual property rights of Biorex and we have licensed additional technologies covered by patents or patent applications, most of which are in the RNAi field.

As part of our development process, we evaluate the patentability of new inventions and improvements developed by us or our collaborators. Whenever appropriate, we will endeavor to file United States and international patent applications to protect these new inventions and improvements. However, we cannot be certain that any of the current pending patent applications we have filed or licensed, or any new patent applications we may file or license, will ever be issued in the United States or any other country. Even if issued, there can be no assurance that those patents will be sufficiently broad to prevent others from using our products or processes. Furthermore, our patents, as well as those we have licensed or may license in the future, may be held invalid or unenforceable by a court, or third parties could obtain patents that we would need to either license or to design around, which we may be unable to do. Current and future competitors may have licensed or filed patent applications or received patents, and may acquire additional patents and proprietary rights relating to molecular chaperone co-induction and other small molecule technology, RNAi technology, DNA-based vaccines or other compounds, products or processes competitive with ours.

In addition to patent protection, we also attempt to protect our proprietary products, processes and other information by relying on trade secrets and non-disclosure agreements with our employees, consultants and certain other persons who have access to such products, processes and information. Under the agreements, all inventions conceived by employees are our exclusive property. Nevertheless, there can be no assurance that these agreements will afford significant protection against misappropriation or unauthorized disclosure of our trade secrets and confidential information.

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Competition

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

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

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

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

Government Regulation

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

The manufacturing facilities and processes for our products, which we anticipate will be manufactured by our strategic partners or licensees or other third parties, will be subject to rigorous regulation, including the need to comply with Federal Good Manufacturing Practice regulations. Our manufacturers also will be subject to regulation under the Occupational Safety and Health Act, the Environmental Protection Act, the Nuclear Energy and Radiation Control Act, the Toxic Substance Control Act and the Resource Conservation and Recovery Act.

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Employees

As of December 31, 2005, we had 28 employees, 18 of whom were engaged in research and development activities and 10 of whom were involved in management and administrative operations. All of the full-time employees engaged in research and development activities hold Ph.D. degrees.

Item 1A. ***Risk Factors***

If any of the following risks actually occur, our business or prospects could be materially adversely affected. You should also refer to the other information in this Annual Report, including our financial statements and the related notes.

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

We have incurred significant losses over the past five years, including net losses of $15.1 million, $16.4 million and $17.8 million for the years ended December 31, 2005, 2004 and 2003, respectively, and we had an accumulated deficit of approximately $121.3 million as of December 31, 2005. Our operating losses have been due primarily to our expenditures for research and development on our products and for general and administrative expenses and our lack of significant revenues. We are likely to continue to incur operating losses until such time, if ever, that we generate significant recurring revenues. We 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 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 $184,000, $428,000, and $94,000 during the years ended December 31, 2005, 2004 and 2003, 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 expect to incur losses from operations until such time, if ever, as we can generate significant recurring revenues. On March 7, 2006, we completed a private placement financing and received net proceeds of approximately $12.4 million. Although we believe that we have adequate financial resources to support our currently planned level of operations into the third quarter of 2007, we will be dependent on obtaining financing from third parties in order to maintain our operations, including our Phase II clinical program with arimoclomol for ALS, our planned levels of operations for our obesity and type 2 diabetes laboratory, our planned RNAi subsidiary and our ongoing research and development efforts related to our other small molecule drug candidates, and in order to continue to meet our obligations to UMMS.

We have no commitments from third parties to provide us with any additional debt or equity financing, and may not be able to obtain future financing on favorable terms, or at all. A lack of needed financing would force us to reduce the scope of, or terminate, our operations, or to seek to merge with or to be acquired by another company. There can be no assurance that we 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 54%, 93% and 81% of our total revenues for the years ended December 31, 2005, 2004 and 2003, 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. Since TranzFect is to be used as a component in

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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 our small molecule drug candidates, and 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 or biotechnology companies for this purpose.

There can be no assurance that any of 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 recently-completed Phase I clinical trial conducted by UMMS and Advanced BioScience Laboratories on an HIV vaccine candidate that utilizes a technology that we licensed from UMMS, 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 may also seek to acquire products from third parties that already are being marketed or have previously been marketed. We have not yet identified any of these products. Even if we do identify such products, it may be difficult for us to acquire them with our limited financial resources and, if we acquire products using our securities as currency, we may incur substantial shareholder dilution. We do not have any prior experience in acquiring or marketing products and may need to find third parties to market these products for us. We may also seek to acquire products through a merger with one or more companies that own such products. In any such merger, the owners of our merger

partner could be issued or hold a substantial, or even controlling, amount of stock in our company or, in the event that the other company is the surviving company, in that other company.

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

In June 2004, we licensed Flocor to SynthRx, which will be responsible for developing potential product applications for Flocor. Although we are not doing any further development work on TranzFect or Flocor, should our three principal licensees for those technologies successfully meet the defined milestones, we could receive future milestone payments and, should any of the licensees

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commercialize products based upon our technology, future royalty payments. However, there can be no assurance that our licensees will continue to develop or ever commercialize any products that are based on our Flocor or our TranzFect technology.

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

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

Under our license for our HIV vaccine candidate, following the completion of the current Phase I trial, we will be responsible for all of the costs for subsequent clinical trials for this vaccine. The costs of subsequent trials for the HIV vaccine will be very substantial. Although we are seeking NIH or other governmental funding for these future trials, we do not have, 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 laboratory, our planned sponsored research funding for Massachusetts General Hospital, our Phase II clinical program with arimoclomol for ALS and our development of our small molecule drug candidates, substantially exceed our current financial resources. Although we raised approximately $12.4 million in March 2006, net of transaction expenses, those required expenditures will nonetheless require us to raise additional capital or to secure a licensee or strategic partner in order to maintain our operations, including our Phase II clinical program with arimoclomol for ALS, our planned levels of operations for our obesity and type 2 diabetes laboratory, our planned RNAi subsidiary and our ongoing research and development efforts related to our other small molecule drug candidates, and in order to continue to meet our obligations to UMMS. If we are unable to meet our 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 laboratory.

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

All of our products 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.

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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 Therapeutics Using RNAi is Unproven and May Never Lead to Marketable Products

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

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

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

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

On October 4, 2004, we acquired all of the clinical and pharmaceutical assets and related intellectual property of Biorex, including three drug candidates (arimoclomol, 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.

In September 2005, we initiated Phase II clinical testing for arimoclomol for ALS. There are no assurances that the clinical testing will be successful, or that the FDA will permit us to commence our planned Phase IIb clinical trial

upon the completion of our ongoing Phase IIa clinical trial. Any additional requirements imposed by the FDA in connection with the ongoing Phase IIa trial, or in connection with our planned Phase IIb trial, could add further time and expense for us to carry out this trial.

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We believe that the FDA may accept the completion of a successful Phase II clinical program as sufficient to enable us to submit a New Drug Application, or NDA; however there are no assurances that the FDA will accept our Phase II program in lieu of a Phase III clinical trial. If the FDA requires us to complete a Phase III clinical trial, the cost of development of arimoclomol will increase significantly beyond our estimated costs, and the time to completion of clinical testing would be delayed. In addition, the FDA ultimately could require us to achieve an efficacy end point in the clinical trials for arimoclomol that could be more difficult, expensive and time-consuming than our planned end point. Although we anticipate developing arimoclomol for the treatment of ALS, arimoclomol has also shown therapeutic efficacy in a preclinical animal model of diabetes and we may pursue development of arimoclomol for diabetic indications. However, such development would require significant and costly additional testing. There is no guarantee that arimoclomol 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 Laboratory May Not Be Able to Develop Products

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

We Will Be Reliant Upon SynthRx to Develop and Commercialize Flocor

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

Our prior Phase III clinical trial of Flocor for the treatment of sickle cell disease patients experiencing an acute vaso-occlusive crisis did not achieve its primary objective. However, in this study, for patients 15 years of age or younger, the number of patients achieving a resolution of crisis was higher for Flocor-treated patients at all time

periods than for placebo-treated patients, which may indicate that future clinical trials should focus on juvenile patients. Generating sufficient data to seek FDA approval for Flocor will require additional clinical studies which have not yet been funded or commenced by SynthRx, and those studies will entail substantial time and expense for SynthRx.

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

We Are Subject to Intense Competition 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, Alnylam Pharmaceuticals, Acuity Pharmaceuticals, Nastech Pharmaceutical Company Inc., Nucleonics, Inc., Benitec Ltd. and a number of the multinational pharmaceutical companies. A number of products currently are being marketed by a variety of the multinational or other pharmaceutical companies for treating type II diabetes, including among others the diabetes drugs Avandia(R) by Glaxo SmithKline PLC, Actos(R) by Eli Lilly & Co., Glucophage(R) by Bristol-Myers Squibb Co., Symlin(R) by Amylin Pharmaceuticals, Inc. and Starlix(R) by Novartis and the obesity drugs Acomplia(R) by Sanofi-Aventis SA, Xenical(R) by F. Hoffman-La Roche Ltd. and Meridia(R) by Abbott Laboratories. Many major pharmaceutical companies are also seeking to develop new therapies for these disease indications. Companies developing HIV vaccines that could compete with our HIV vaccine technology include Merck, VaxGen, Inc., AlphaVax, Inc. and Immunitor Corporation.

Currently, Rilutek(R), which was developed by Aventis Pharma AG, is the only drug of which we are aware that has been approved by the FDA for the treatment of ALS. Other companies are working to develop pharmaceuticals to treat ALS, including Aeolus Pharmaceuticals, Ono Pharmaceuticals, Trophos SA, FaustPharmaceuticals SA and Oxford BioMedica plc. In addition, ALS belongs to a family of diseases called neurodegenerative diseases, which

includes Alzheimer s, Parkinson s and Huntington s disease. Due to similarities between these diseases, a new treatment for one ailment potentially could be useful for treating others. There are many companies that are producing and developing drugs used to treat neurodegenerative diseases other than ALS, including Amgen, Inc., Cephalon, Inc., Ceregene, Inc., Elan Pharmaceuticals, plc, H. Lundbeck A/S, Phytopharm plc, and Schwarz Pharma AG.

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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(R) (hydroxyurea) marketed by Bristol-Myers Squibb Co. and Dacogen(tm), 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(tm) marketed by Antigenics, Inc. and adjuvants marketed by Corixa Corp.

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

We do not currently have the facilities or expertise to manufacture any of the clinical or commercial supplies of any of our products, including the supply of arimoclomol used in our Phase II clinical trials. Accordingly, we are and will be dependent upon contract manufacturers or our strategic alliance partners to manufacture these supplies, or we will need to acquire the ability to manufacture these supplies ourselves, which could be very difficult, time-consuming and costly. We have a manufacturing supply arrangement in place with respect to the clinical supplies for both the Phase IIa and Phase IIb trials for arimoclomol for ALS. We do not otherwise have manufacturing supply arrangements for our other product candidates, including any of the licensed RNAi technology, the other 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. In particular, although we conducted certain due diligence regarding the patents and patent applications acquired from Biorex and received certain representations and warranties from Biorex in connection with the acquisition, the patents and patent applications acquired from Biorex were issued or filed, as applicable, prior to our acquisition and thus there can be no assurance that the validity, enforceability and ownership of those patents and patent applications will be upheld if challenged by third parties. We have a nonexclusive license to a patent owned by UMMS and the Carnegie Institution of Washington that claims various aspects of gene silencing, or genetic inhibition by double-stranded RNA, but there can be no assurance that this patent will withstand possible third-party challenges or otherwise protect our technologies from competition. The medical applications of the gene silencing technology and the other technologies that we have licensed from 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.

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

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

If any of our products are alleged to be defective, they may expose us to claims for personal injury by patients in clinical trials of our products or by patients using our commercially marketed products. Even if the commercialization of one or more of our products is approved by the FDA, users may claim that such products caused unintended adverse effects. We currently do not carry product liability insurance covering the commercial marketing of these products. We have obtained clinical trial insurance for our recently-initiated Phase IIa clinical trial with arimoclomol for the treatment of ALS and will seek to obtain such insurance for any other clinical trials that we conduct, including the planned Phase IIb clinical trial for arimoclomol, as well as liability insurance for any products that we market, although there can be no assurance that we will be able to obtain additional insurance in the amounts we seek or at all. We anticipate that our licensees who are developing our products will carry liability insurance covering the clinical testing and marketing of those products. However, 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.

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

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

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

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

We have a classified board of directors, which requires that at least two stockholder meetings, instead of one, will be required to effect a change in the majority control of our board of directors. This provision applies to every election

of directors, not just an election occurring after a change in control. The classification of our board increases the amount of time it takes to change majority control of our board of directors and may cause our potential purchasers to lose interest in the potential purchase of us, regardless of whether our purchase would be beneficial to us or our stockholders. The additional time and cost to change a majority of the members of our board of directors makes it more difficult and may discourage our existing stockholders from seeking to change our existing management in order to change the strategic direction or operational performance of our company.

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

In August 2003, we registered with the SEC for resale by the holders a total of 14,408,252 shares of our outstanding common stock and an additional 3,848,870 shares of our common stock issuable upon exercise of outstanding options and warrants, which shares and options and warrants were issued primarily in connection with our merger with Global Genomics and the $5.4 million private equity financing that we completed in May 2003. In December 2003, we registered a total of 6,113,448 shares of our common stock, consisting of the 5,175,611 shares issued, or that are issuable upon exercise of the warrants issued, in connection with the $8.7 million private equity financing that we completed in September 2003, and an additional 937,837 shares of our common stock that we issued, or that are issuable upon the exercise of warrants that we issued, to certain other third parties. In November 2004, we registered 4,000,000 shares of our common stock and an additional 3,080,000 shares of our common stock issuable upon the exercise of warrants in connection with the $4,000,000 private equity financing that we completed in October 2004, and an additional 1,550,000 shares of our common stock issued or issuable upon exercise of warrants to other third parties. In February 2005, we registered 17,334,494 shares of our common stock and an additional 9,909,117 shares of our common stock issuable upon the exercise of warrants in connection with the $21.3 million private equity financing that we completed in January 2005. In April 2006, we expect to file a registration statement to register 10,650,794 shares of our common stock and an additional 5,325,397 shares of our common stock issuable upon the exercise of warrants in connection with the $13.4 million private equity financing that we completed in March 2006. 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 first quarter of 2006. We

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

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

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

Our quarterly operating results.

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

Government regulation of drug pricing.

Developments in patent or other technology ownership rights.

Public concern regarding the safety of our products.

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

Item 2. ***Properties***

Our operations are based in Los Angeles, California, and Worcester, Massachusetts. The lease for our headquarters facility in Los Angeles covers approximately 4,700 square feet of office space and expires in June 2008. The lease for our laboratory in Worcester covers approximately 6,900 square feet of office and laboratory space and expires in December 2007. Our facilities are suitable and adequate for our current operations.

Item 3. ***Legal Proceedings***

We are occasionally involved in claims arising out of our operations in the normal course of business, none of which are expected, individually or in the aggregate, to have a material adverse effect on us.

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PART II

Item 5. ***Market for Registrant s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities***

Our common stock is currently traded on the Nasdaq Capital Market under the symbol CYTR. The following table sets forth the high and low sale prices for our common stock for the periods indicated as reported by the Nasdaq Capital Market.

	High	Low
Fiscal Year 2006:		
January 1 to March 28	$1.87	$1.01
Fiscal Year 2005:		
Fourth Quarter	$1.13	$0.85
Third Quarter	$1.22	$0.76
Second Quarter	$1.44	$0.75
First Quarter	$2.07	$1.14
Fiscal Year 2004:		
Fourth Quarter	$1.75	$1.10
Third Quarter	$1.80	$0.94
Second Quarter	$2.10	$1.06
First Quarter	$2.43	$1.43

On March 15, 2006, there were approximately 10,900 holders of record of our common stock. The number of record holders does not reflect the number of beneficial owners of our common stock for whom shares are held by brokerage firms and other institutions. We have not paid any dividends since our inception and do not contemplate paying dividends in the foreseeable future.

Item 6. ***Selected Financial Data***

The following selected financial data are derived from our audited financial statements. Our financial statements for 2005, 2004 and 2003 have been audited by BDO Seidman, LLP, our independent registered public accounting firm. These historical results do not necessarily indicate future results. When you read this data, it is important that you also read our financial statements and related notes, as well as the section Management s Discussion and Analysis of Financial Condition and Results of Operations and Risk Factors. Financial information provided below has been rounded to the nearest thousand.

	2005	2004	2003	2002	2001
Statement of Operations Data:					
Revenues					
Recruiting revenues	$	$	$	$ 23,000	$ 101,000
License fees	101,000	428,000	94,000	1,051,000	3,751,000
Grant income				46,000	157,000
Service revenues	83,000				
Total revenues	$ 184,000	$ 428,000	$ 94,000	$ 1,120,000	$ 4,009,000
Net loss	$ (15,093,000)	$ (16,392,000)	$ (17,845,000)	$ (6,176,000)	$ (931,000)
Basic and diluted loss per common share:					
Net loss	$ (0.27)	$ (0.48)	$ (0.65)	$ (0.39)	$ (0.09)

Balance Sheet Data:					
Total assets	$ 9,939,000	$ 5,049,000	$ 12,324,000	$ 9,284,000	$ 7,611,000
Total stockholders equity	$ 7,208,000	$ 1,595,000	$ 10,193,000	$ 7,959,000	$ 6,583,000

In March 2006, we completed a $13.4 million private equity financing in which we issued 10,650,794 shares of our common stock and warrants to purchase an additional 5,325,397 shares of our common stock at an exercise price of $1.54 per share. Net of investment banking commissions, legal, accounting and other fees related to the transaction, we received proceeds of approximately $12.4 million.

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Factors Affecting Comparability

In January 2005, we completed a $21.3 million private equity financing in which we issued 17,334,494 shares of our common stock and warrants to purchase an additional 8,667,247 shares of our common stock at an exercise price of $2.00 per share. Net of investment banking commissions, legal, accounting and other fees related to the transaction, we received proceeds of approximately $19.4 million.

In the fourth quarter of 2004, we completed our acquisition of all of the clinical, pharmaceutical and related intellectual property assets of Biorex, a Hungary-based company focused on the development of novel small molecules with broad therapeutic applications in neurology, diabetes and cardiology. We paid Biorex $3.0 million in cash for the assets at the closing, and incurred approximately $500,000 in expenses related to the transaction.

The assets acquired from Biorex include three drug candidates that had completed the equivalent of a Phase I clinical trial. We intend to perform additional testing on those drug candidates, and initiated a Phase II clinical trial for one of the drug candidates, arimoclomol, for ALS in September 2005. In addition, we acquired a 500-compound molecular library, which we plan to use in high throughput screening at our obesity and diabetes laboratory. With the assistance of an outside appraiser, we evaluated the technology assets acquired from Biorex, including their current state of development, the severability of the assets, and alternative uses of the compounds. Based in part on that appraisal, we concluded that the $3.0 million value allocated to the three drug candidates should be written off at the time of acquisition as in-process research and development, and that the $500,000 value attributable to the 500-compound molecular library should be included in our fixed assets at December 31, 2004.

In the third quarter of 2003, we recorded an impairment charge of $5.9 million related to our investments in Blizzard s acquired developed technology and in Psynomics, based upon our analysis of the recoverability of the carrying amount of these assets in accordance with the Accounting Principles Board Opinion No. 18, The Equity Method of Accounting for Investments in Common Stock. This impairment charge represented the total net book value of these assets at the time of the write-off. See Note 12 to our audited financial statements.

Item 7. ***Management s Discussion and Analysis of Financial Condition and Results of Operations***

The following discussion and analysis of our financial condition and results of operations should be read together with the discussion under Selected Financial Data and our consolidated financial statements included in this Annual Report. This discussion contains forward-looking statements, based on current expectations and related to future events and our future financial performance, that involve risks and uncertainties. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of many important factors, including those set forth under Risk Factors and elsewhere in this Annual Report.

Restatement of Financial Statements

We have restated our consolidated financial statements for the year ended December 31, 2005 and each of the quarters ended March 31, 2005, June 30, 2005, and September 30, 2005, respectively. The restatements are related to the pro forma amounts disclosed in accordance with SFAS 123, *Accounting for Stock-Based Compensation,* which were calculated incorrectly as set forth in the stock-based compensation sections of the footnotes contained in our consolidated financial statements for these periods. The restatement also includes a correction in the accounting for antidilution features in certain of our outstanding warrants. On May 20, 2006, the Audit Committee of our Board of Directors approved management s recommendation to restate our consolidated financial statements for these periods to reflect the corrected disclosures in our stock-based compensation footnote and the correction in the accounting for antidilution features in certain of our outstanding warrants.

The following discussion gives effect to the restatements. See Notes 2 and 14 to Consolidated Financial Statements contained herein.

Overview

We are in the process of developing products, primarily in the areas of small molecule therapeutics and ribonucleic acid interference, or RNAi, for the human health care market. Our small molecule therapeutics efforts include our clinical development of three oral drug candidates that we acquired in October 2004, including a Phase II trial initiated in September 2005, as well as our drug discovery operations conducted at our laboratory in Worcester, Massachusetts. Development work on RNAi, a relatively recent technology for silencing genes in living cells and organisms, is still at an early stage, and we are aware of only four clinical tests of

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therapeutic applications using RNAi that have yet been initiated by any party. In addition to our work in RNAi and small molecule therapeutics, we recently announced that a novel HIV DNA + protein vaccine exclusively licensed to us and developed by researchers at the University of Massachusetts Medical School, or UMMS, and Advanced BioScience Laboratories, and funded by the National Institutes of Health, demonstrated promising interim Phase I clinical trial results that indicate its potential to produce potent antibody responses with neutralizing activity against multiple HIV viral strains. We have also entered into strategic alliances with respect to the development of several other products using our other technologies.

On October 4, 2004, we acquired all of the clinical and pharmaceutical and related intellectual property assets of Biorex Research & Development, RT, or Biorex, a Hungary-based company focused on the development of novel small molecules based on molecular chaperone co-induction technology, with broad therapeutic applications in neurology, type 2 diabetes, cardiology and diabetic complications. The acquired assets include three oral, clinical stage drug candidates and a library of 500 small molecule drug candidates. We recently entered the clinical stage of drug development with the initiation of a Phase II clinical program with our lead small molecule product candidate arimoclomol for the treatment of ALS. Arimoclomol has received Orphan Drug and Fast Track designation from the U.S. Food and Drug Administration.

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

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

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

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

We have no significant revenues and we expect not to have significant revenues and to continue to incur significant losses over the next several years. Our net losses may increase from current levels primarily due to activities related to

our collaborations, technology acquisitions, ongoing and planned clinical trials, research and development programs and other general corporate activities. We anticipate that our operating results will fluctuate for the foreseeable future. Therefore, period-to-period comparisons should not be relied upon as predictive of the results in future periods.

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To date, we have relied primarily upon sales of equity securities and, to a much lesser extent, upon payments from our strategic partners and licensees and upon proceeds received upon the exercise of options and warrants, to generate the funds needed to finance our business plans and operations. We will be required to obtain significant additional funding in order to execute our long-term business plans. Our sources of potential funding for the next several years are expected to consist primarily of proceeds from sales of equity, but could also include license and other fees, funded research and development payments, gifts and grants, and milestone payments under existing and future collaborative arrangements. However, we have no commitment or arrangements for such additional funding.

Research and Development

Following our 2003 acquisition of rights to new technologies from UMMS and our 2004 acquisition of the clinical assets of Biorex, we initiated research and development programs for products based upon those technologies. Expenditures for research and development activities related to continuing operations were $9.1 million, $9.0 million and $4.4 million for the years ended December 31, 2005, 2004 and 2003, respectively, with research and development expenses representing approximately 58%, 53% and 39% of our total expenses for the years ended December 31, 2005, 2004 and 2003, respectively. Included in research and development expenses for 2004 was $3.0 million of in-process research and development that was written off in conjunction with our acquisition of assets from Biorex. Research and development expenses are further discussed below under Critical Accounting Policies and Estimates and Results of Operations.

There is a risk that any drug discovery and development program may not produce revenue because of the risks inherent in drug discovery and development. Moreover, there are uncertainties specific to any new field of drug discovery, including molecular chaperone co-induction technology or RNAi. The successful development of any product candidate we develop is highly uncertain. We cannot reasonably estimate or know the nature, timing and costs of the efforts necessary to complete the development of, or the period in which material net cash inflows are expected to commence from any product candidate, due to the numerous risks and uncertainties associated with developing drugs, including the uncertainty of:

Our ability to advance product candidates into pre-clinical and clinical trials.

The scope, rate and progress of our pre-clinical trials and other research and development activities.

The scope, rate of progress and cost of any clinical trials we commence.

The cost of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights.

Future clinical trial results.

The terms and timing of any collaborative, licensing and other arrangements that we may establish.

The cost and timing of regulatory approvals.

The cost and timing of establishing sales, marketing and distribution capabilities.

The cost of establishing clinical and commercial supplies of our product candidates and any products that we may develop.

The effect of competing technological and market developments.

Any failure to complete any stage of the development of our products in a timely manner could have a material adverse effect on our operations, financial position and liquidity. A discussion of the risks and uncertainties associated with completing our projects on schedule, or at all, and the potential consequences of failing to do so, are set forth in the Risk Factors section of this Annual Report.

Critical Accounting Policies and Estimates

Management s discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires management to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses, and related disclosure of contingent assets and liabilities. On an ongoing basis, management

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evaluates its estimates, including those related to revenue recognition, bad debts, impairment of long-lived assets, including finite lived intangible assets, accrued liabilities and certain expenses. We base our estimates on historical experience and on various other assumptions that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ materially from these estimates under different assumptions or conditions.

Our significant accounting policies are summarized in Note 2 to our audited financial statements. We believe the following critical accounting policies affect our more significant judgments and estimates used in the preparation of our consolidated financial statements:

Revenue Recognition

Nonrefundable license fee revenue is recognized when collectibility is reasonably assured, which is generally upon receipt, when no continuing involvement on our part is required and payment of the license fee represents the culmination of the earnings process. Nonrefundable license fees received subject to future performance by us, or that are credited against future payments due to us are deferred and recognized as services are performed and collectibility is reasonably assured, which is generally upon receipt, or upon termination of the agreement and all related obligations thereunder, whichever is earlier. Our revenue recognition policy may require us in the future to defer significant amounts of revenue.

Research and Development Expenses

Research and development expenses consist of costs incurred for direct and overhead-related research expenses and are expensed as incurred. Costs to acquire technologies which are utilized in research and development and which have no alternative future use are expensed when incurred. Technology developed for use in our products is expensed as incurred, until technological feasibility has been established. Expenditures, to date, have been classified as research and development expense in the consolidated statements of operations and we expect to continue to expense research and development for the foreseeable future.

Clinical Trial Expenses

Clinical trial expenses, which are included in research and development expenses, include obligations resulting from our contracts with various clinical research organizations in connection with conducting clinical trials for our product candidates. We recognize expenses for these activities based on a variety of factors, including actual and estimated labor hours, clinical site initiation activities, patient enrollment rates, estimates of external costs and other activity-based factors. We believe that this method best approximates the efforts expended on a clinical trial with the expenses we record. We adjust our rate of clinical expense recognition if actual results differ from our estimates.

Stock-based Compensation

We apply Accounting Principles Board Opinion No. 25 (APB 25), *Accounting for Stock Issued to Employees*, and related interpretations in accounting for our stock-based employee compensation plans, rather than the alternative fair value accounting method provided for under Statement of Financial Accounting Standards No. 123, *Accounting for Stock-Based Compensation* (SFAS 123). In the Notes to Consolidated Financial Statements, we provide pro forma disclosures in accordance with SFAS 123 and related pronouncements. Under APB 25, compensation expense is recorded on the date of grant of an option to an employee or member of the Board only if the fair market value of the underlying stock at the date of grant exceeds the exercise price. In addition, we have granted options to certain outside consultants, which are required to be measured at fair value and recognized as compensation expense in our financial statements. We apply the Black-Scholes option-pricing model for estimating the fair value of options, which involves a number of judgments and variables, including estimates of the life of the options and expected volatility which are subject to significant change. A change in the fair value estimate could have a significant effect on the amount of pro forma compensation expense calculated.

In December 2004, the FASB released its revised standard, SFAS No. 123(R) (SFAS 123(R)), Share-Based Payment. SFAS 123(R) requires that a public entity measure the cost of equity-based service awards based on the fair value of the award on the date of grant. That cost will be recognized over either the vesting period or the period during which an employee is required to provide service in exchange for the award. We are required to adopt the provisions of SFAS 123(R) for periods after January 2006, and we will adopt the new requirements using the modified

prospective transition method. The adoption of SFAS 123(R) requires us to value stock options granted prior to adoption of SFAS 123(R) under the fair value method and expense these amounts in the income statement over the stock option s remaining vesting period. The adoption of SFAS 123(R) will result in recognition of additional non-

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cash stock-based compensation expense and, accordingly, will increase net losses in amounts which likely will be considered material, although it will not impact our cash position.

We account for equity instruments issued to non-employees in accordance with the provisions of SFAS 123 and Emerging Issues Task Force Issue (EITF) No. 96-18, *Accounting for Equity Instruments that Are Issued to other than Employees for Acquiring, or in conjunction with Selling Goods, or Services* (EITF 96-18) which require that such equity instruments are recorded at their fair value on the measurement date. The measurement of stock-based compensation is subject to periodic adjustment as the underlying equity instruments vest. Non-employee stock-based compensation charges are amortized over the vesting period on a straight-line basis.

Impairment of Long-Lived Assets

We review long-lived assets, including finite lived intangible assets, for impairment on an annual basis, as of December 31, or on an interim basis if an event occurs that might reduce the fair value of such assets below their carrying values. An impairment loss would be recognized based on the difference between the carrying value of the asset and its estimated fair value, which would be determined based on either discounted future cash flows or other appropriate fair value methods.

In accordance with the provisions of Accounting Principles Board Opinion No. 18, *The Equity Method of Accounting for Investments in Common Stock* (APB 18), we reviewed the net values on our balance sheet, as of September 30, 2003, assigned to Investment in Minority Owned Entity Acquired Developed Technology resulting from our acquisition of Blizzard Research and Development Company, or Blizzard. Blizzard was recorded as an acquired development-stage company and there was an external valuation used for substantiation of the value of the technology and the investment, which was prepared as of the date of the announcement of the transaction February 11, 2002. For our annual audit of fiscal 2002, potential impairment was addressed and the valuation was updated internally using similar methods used for the original investment. Based upon our analysis there was no impairment. Our auditors for that fiscal year concurred. We continued to measure impairment through these methods on a quarterly basis and through the second quarter of 2003, we continued to believe that Blizzard s proprietary technology was commercially viable, subject to its ability to obtain significant financing. At that time we believed there was no impairment. APB 18 requires that a loss in value of an investment, which is other than a temporary decline, should be recognized as an impairment loss. Through the third quarter of 2003, Blizzard had been unsuccessful in its attempts to raise a significant amount of financing necessary for it to pursue its commercialization strategy for its products and we subsequently decided not to further invest in this entity. We believe that Blizzard was unable to obtain substantial third-party financing primarily because (1) the genomics market, which the Blizzard technology was targeting, had begun to decline in 2003, (2) Blizzard had not completed a production unit of its principal product for testing by potential investors, and (3) certain investors were unwilling to invest without a simultaneous infusion of additional capital from us as Blizzard s 40% shareholder, and we were unable to reach satisfactory terms for such financing. Our analysis consisted of a review of the financial projections prepared by Blizzard, application of a discounted cash flow valuation model of Blizzard s projected cash flows, and consideration of other qualitative factors such as Blizzard s termination of its employees, its office lease and its engagement of its investment banker. Based upon the quantitative and qualitative factors described above, in addition to others, our management determined that the estimated fair value of our investment in Blizzard was $0 and that an impairment charge of $5.9 million was necessary. In considering the timing of the write-off, we looked to Blizzard s termination of its employees, lease and investment banker in October 2003 as affirmation of conditions that existed at September 2003, and therefore recorded the write-off in the third quarter of 2003. The write-off had no impact upon our cash or working capital position. It is our understanding that, by the end of 2003, Blizzard had ceased operations and, in 2004, returned its licensed intellectual property to the Minnesota Research Fund.

Estimated Facility Abandonment Accrual

Subsequent to our merger with Global Genomics in 2002, we recorded a loss of $563,000 associated with the closure of our Atlanta headquarters and our relocation to Los Angeles. This loss represented the total remaining lease obligations and estimated operating costs through the remainder of the lease term, less estimated sublease rental income and deferred rent at the time. In August 2005, we entered into a lease termination agreement pursuant to which we were released from all future obligations on the lease in exchange for a one-time $110,000 payment and the

forfeiture of a $49,000 security deposit. As a result of this agreement, we realized a $164,000 offset against third quarter general and administrative expenses.

Quarterly Financial Data

The following table sets forth unaudited statement of operations data for our most recent two completed fiscal years. This quarterly information has been derived from our unaudited financial statements and, in the opinion of management, includes all adjustments, consisting only of normal recurring adjustments, necessary for a fair presentation of the information for the periods covered. The

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quarterly financial data should be read in conjunction with our financial statements and related notes. The operating results for any quarter are not necessarily indicative of the operating results for any future period.

	Quarter Ended			
	March 31	June 30	September 30	December 31
	(In thousands, except per share data)			
2005				
Total revenues	$ 1	$	$ 10	$ 173
Net loss	(3,527)	(4,509)	(3,492)	(3,565)
Basic and diluted loss per common share:				
Net loss	$ (0.07)	$ (0.08)	$ (0.06)	$ (0.06)
2004				
Total revenues	$ 100	$ 228	$	$ 100
Net loss	(3,774)	(4,061)	(2,796)	(5,761)
Basic and diluted loss per common share:				
Net loss	$ (0.11)	$ (0.12)	$ (0.08)	$ (0.15)

Quarterly and year to date loss per share amounts are computed independently of each other. Therefore, the sum of the per share amounts for the quarters may not agree to the per share amounts for the year.

Liquidity and Capital Resources

At December 31, 2005, we had cash, cash equivalents and short-term investments of $8.3 million and total assets of $9.9 million compared to $3.0 million and $5.0 million, respectively, at December 31, 2004. Working capital totaled $6.3 million at December 31, 2005, compared to $1.2 million at December 31, 2004.

To date, we have relied primarily upon sales of equity securities and, to a much lesser extent, payments from our strategic partners and licensees and upon proceeds received upon the exercise of options and warrants, to generate funds needed to finance our business and operations. As a result of the $12.4 million equity financing, net of expenses, that we completed in March 2006, we believe that we have adequate working capital to support our currently planned level of operations into the third quarter of 2007, including our current and planned clinical trials for arimoclomol, drug discovery efforts related to additional product candidates, working capital and general corporate purposes. Included in our planned expenses are approximately $3.2 million for our Phase II clinical program with arimoclomol for ALS during 2006, and an additional $4.5 million in 2007 and $6.3 million in 2008. The cost of our clinical program for ALS could vary significantly from our current projections due to any additional requirements imposed by the FDA in connection with the ongoing Phase IIa trial, or in connection with our planned Phase IIb trial, or if actual costs are higher than current management estimates for other reasons. In the event that actual costs of our clinical program for ALS, or any of our other ongoing research activities, are significantly higher than our current estimates, we may be required to significantly modify our planned level of operations. In the future, we will be dependent on obtaining financing from third parties in order to maintain our operations, including our Phase II clinical program with arimoclomol for ALS, our planned levels of operations for our obesity and type 2 diabetes research laboratory and our ongoing research and development efforts related to our other small molecule drug candidates, and in order to continue to meet our obligations to UMMS. We currently have no commitments from any third parties to provide us with capital. We cannot assure that additional funding will be available to us on favorable terms, or at all. If we fail to obtain additional funding when needed, we would be forced to scale back, or terminate, our operations, or to seek to merge with or to be acquired by another company.

For the year ended December 31, 2005, net cash provided by investing activities consisted of $964,000, of which $1.0 million was from the redemption of short-term securities, which was partially offset by the acquisition of $48,000 of property and equipment. We expect capital spending to increase during 2006 over our 2005 levels to support our increasing research and development efforts and the implementation of Sarbanes-Oxley. In the year ended December 31, 2004, net cash used in investing activities consisted of $962,000 for the purchase of securities to be held to maturity and $772,000 for property and equipment, which includes $447,000 related to assets acquired in

connection with the molecular library assets of Biorex. Net cash provided by investing activities for the year ended December 31, 2003 was $1.2 million which was primarily due to the maturity of held-to-maturity investments acquired in 2002.

Cash provided by financing activities for the year-ended December 31, 2005 was $19.8 million. The cash provided includes $256,000 received upon the exercise of stock options and warrants. Additionally, we raised $19.6 million through the sale of equity, of which $19.4 million was raised in connection with a private equity financing, net of expenses, that closed in January 2005. Net cash

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provided by financing activities in the year ended December 31, 2004 was $4.4 million. The cash provided was the result of $526,000 received upon the exercise of stock options and warrants and the $4.0 million private equity financing completed in October 2004. Net cash provided by financing activities for the year ended December 31, 2003 was $14.4 million. In May and September 2003, we completed private equity financings raising net proceeds of $4.9 million and $7.7 million, respectively. For the year ended December 31, 2003, we also received proceeds from the exercise of stock options and warrants totaling $1.9 million.

Our net loss for the year-ended December 31, 2005 was $15.1 million, which resulted in net cash used in operating activities of $14.5 million. Adjustments to reconcile net loss to net cash used in operating activities for the year-ended December 31, 2005 include $586,000 of common stock, options and warrants issued in lieu of cash for research and development and general and administrative services, as well as a net change in assets and liabilities of $210,000 offset by the recording of $217,000 in depreciation and amortization. Our net loss for the year ended December 31, 2004 was $16.4 million, which includes the write-off of $3.0 million of in-process research and development related to the acquisition of assets from Biorex. The $16.4 million loss resulted in net cash used in operating activities of $12.4 million. Adjustments to reconcile net loss to net cash used in operating activities for the year ended December 31, 2004 were primarily $873,000 of common stock, options and warrants issued in lieu of cash for general and administrative services. Additionally, we issued $388,000 of common stock, options and warrants in lieu of cash in connection with certain license fees and $1.0 million in connection with research and development activities. Our net loss for the year-ended December 31, 2003 was $17.8 million, which resulted in net cash used in operating activities of $4.3 million. Adjustments to reconcile net loss to net cash used in operating activities for the year ended December 31, 2003 were primarily $6.7 million of losses from a minority-owned entity, $1.5 million of common stock, options and warrants issued in lieu of cash for general and administrative services, $1.8 million of common stock issued in connection with certain license agreements and $1.1 million of common stock issued in connection with research and development activities.

We believe that we have adequate working capital to allow us to operate at our currently planned levels into the third quarter of 2007. Our strategic alliance with UMMS may require us to make significant expenditures to fund research at UMMS relating to developing therapeutic products based on UMMS s proprietary gene silencing technology that has been licensed to us. The aggregate amount of these expenditures was approximately $2.5 million during 2005, and if we retain our current license portfolio, we expect expenditures to be approximately $1.2 million during 2006.

We will require significant additional capital in order to fund the completion of our Phase II clinical program with our lead small molecule product candidate arimoclomol for the treatment of ALS, which commenced in September 2005, and the other ongoing research and development related to the drug candidates acquired from Biorex in October 2004. We spent $3.8 million on the arimoclomol clinical program in 2005, and we estimate that the overall program, including the ongoing Phase IIa trial and the planned Phase IIb trial that we expect to initiate soon after completion of the present Phase IIa trial subject to FDA approval, will require us to expend approximately $3.2 million in 2006, and an additional $10.8 million over the following 12 to 18 months. However, we may incur substantial additional expense and the trial may be delayed if the FDA requires us to generate additional pre-clinical or clinical data in connection with the clinical trial, or the FDA requires us to revise significantly our planned protocol for the Phase IIb.

Any additional capital may be provided by potential milestones payments pursuant to our licenses with Merck and Vical, both of which relate to Tranzfect, or our license with SynthRx related to Flocor, or by potential payments from future strategic alliance partners or licensees of our technologies. However, Merck is at an early stage of clinical trials of a product utilizing TransFect and Vical has only recently commenced a Phase IIa clinical trial of a product using TransFect, so there is likely to be a substantial period of time, if ever, before we receive any further significant payments from Merck or Vical.

We intend also to pursue other sources of capital, although we do not currently have commitments from any third parties to provide us with capital. The results of our technology licensing efforts and the actual proceeds of any fund-raising activities will determine our ongoing ability to operate as a going concern. Our ability to obtain future financings through joint ventures, product licensing arrangements, equity financings, gifts, and grants or otherwise is

subject to market conditions and out ability to identify parties that are willing and able to enter into such arrangements on terms that are satisfactory to us. Depending upon the outcome of our fundraising efforts, the accompanying financial information may not necessarily be indicative of future operating results or future financial condition.

We expect to incur significant losses for the foreseeable future and there can be no assurance that we will become profitable. Even if we become profitable, we may not be able to sustain that profitability.

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Contractual Obligations

We have no current commitments for capital expenditures in 2006; however, we anticipate incurring capital expenditures in connection with the expansion of our laboratory. As of December 31, 2005, we had no committed lines of credit or other committed funding or long-term debt. As of December 31, 2005, minimum annual future obligations for operating leases, minimum annual future obligations under various license agreements and minimum annual future obligations under employment agreements consist of the following:

	Operating Leases	License Agreements	Employment Agreements	Total
		(In thousands)		
2006	$ 507	$ 971	$ 1,264	$ 2,742
2007	389	235	887	1,511
2008	108	339	590	1,037
2009	1	339		340
2010 and thereafter	2	1070		1,072
Total	$ 1,007	$ 2,954	$ 2,741	$ 6,702

We have employment agreements with our executive officers, the terms of which expire at various times through July 2008. Certain agreements provide for minimum salary levels, which are subject to increase annually in the Compensation Committee s discretion, as well as for minimum annual bonuses. The reported commitment for employment agreements includes, among other things, a total of $0.9 million of compensation payable to members of our Scientific Advisory Board through 2008, and a total of $1.6 million of minimum salary and guaranteed bonuses payable to our executives.

License and Collaboration Agreements

In April 2003, we acquired new technologies by entering into exclusive license arrangements with UMMS covering potential applications of the medical institution s proprietary RNAi technology in the treatment of specified diseases, including those within the areas of obesity, type 2 diabetes ALS and CMV. In consideration of the licenses, we made cash payments to UMMS totaling $186,000 and issued it a total of 1,613,258 shares of our common stock which were valued, for financial statement purposes, at $1.5 million. 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 consideration of this license, we made cash payments to UMMS totaling $18,000 and issued it 215,101 shares of our common stock which were valued, for financial statement purposes, at $361,000. In July 2004, we further expanded our strategic alliance with UMMS by entering into a collaboration and invention disclosure agreement with UMMS under which UMMS will disclose to us certain new technologies developed at UMMS over a three-year period pertaining to RNAi, diabetes, obesity, neurodegenerative diseases (including ALS) and CMV and will give the Company an option, upon making a specified payment, to negotiate an exclusive worldwide license to the disclosed technologies on commercially reasonable terms. Approximately one year remains on the technology disclosure option. As of December 31, 2005, we have made cash payments to UMMS totaling $1.1 million pursuant to the collaboration agreement with UMMS, but have not yet acquired or made any payments to acquire any options under that agreement.

In May 2004, we licensed from the technology transfer company of the Imperial College of Science, Technology & Medicine, or Imperial College, 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. In consideration of the license, we made cash payments to Imperial College totaling $87,000 and issued it a total of 75,000 shares of our common stock which were valued, for financial statement purposes, at the then-aggregate fair market value of $108,000. As the drug screening technology from Imperial College and the RNAi technology from UMMS had not achieved technological feasibility at the time of their license by us, had no alternative future uses and, therefore, no separate economic value, the total value of all cash payments and stock issued for acquisition of the technology was

expensed as research and development in our financial statements.

Net Operating Loss Carryforward

At December 31, 2005, we had consolidated net operating loss carryforwards for income tax purposes of $35.6 million, which will expire in 2006 through 2025 if not utilized. We also have research and development tax credits and orphan drug tax credits available to reduce income taxes, if any, of $6.4 million, which will expire in 2006 through 2025 if not utilized. The amount of net operating loss carryforwards and research tax credits available to reduce income taxes in any particular year may be limited in certain circumstances. Based on an assessment of all available evidence including, but not limited to, our limited operating history in our core

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business and lack of profitability, uncertainties of the commercial viability of our technology, the impact of government regulation and healthcare reform initiatives, and other risks normally associated with biotechnology companies, we have concluded that it is more likely than not that these net operating loss carryforwards and credits will not be realized and, as a result, a 100% deferred tax valuation allowance has been recorded against these assets.

Results of Operations

CytRx Corporation recorded net losses of $15.1 million, $16.4 million and $17.8 million during the years ended 2005, 2004 and 2003.

We earned an immaterial amount in licensing fees during the years ended 2005, 2004 and 2003. All future licensing fees under out current licensing agreements are dependent upon successful development milestones being achieved by the licensor. During fiscal 2006, we are not anticipating receiving any significant licensing fees.

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Research and Development

	Year Ended December 31,		
	2005	2004	2003
		(In thousands)	
Research and development expense	$ 8,867	$ 4,626	$ 1,485
Non-cash research and development expense	220	1,387	2,903
Acquired in-process research and development expense		3,022	
	$ 9,087	$ 9,035	$ 4,388

Research expenses are expenses incurred by us in the discovery of new information that will assist us in the creation and the development of new drugs or treatments. Development expenses are expenses incurred by us in our efforts to commercialize the findings generated through our research efforts. Our research and development expenses were $9.1 million in 2005, $9.0 million in 2004 and $4.4 million in 2003.

Research and development expenses incurred during 2005 relate primarily to (i) the initiation of our Phase II clinical program for arimoclomol in ALS, (ii) our ongoing research and development related to other drug candidates purchased from Biorex, (iii) our research and development activities conducted at UMMS related to the technologies covered by the UMMS license agreements, (iv) our collaboration and invention disclosure agreement pursuant to which UMMS has agreed to disclose certain inventions to us and provide us with the right to acquire an option to negotiate exclusive licenses for those disclosed technologies, and (v) the on-going small molecule drug discovery operations at our Massachusetts laboratory. Although our future research and development activities could vary substantially, our research and development activities will remain substantial in the future as a result of commitments related to the foregoing activities. Research and development expenses presented in the accompanying consolidated financial statements during 2004 were primarily the result of efforts to develop RNAi through new and existing licensing agreements, sponsored research agreements, as well as research and development efforts performed at our Massachusetts laboratory. Research and development expenses incurred in 2003 were primarily for the acquisition and licensing of intellectual property and the commencement of operations of our Massachusetts laboratory. All research and development costs related to the activities of our laboratory are expensed. No in-process research and development costs were eligible for capitalization at the time we purchased the minority interest in our prior subsidiary, CytRx Laboratories.

In October 2004, we acquired all of the clinical and pharmaceutical and related intellectual property assets of Biorex, a Hungry-based company focused on the development of novel small molecules with broad therapeutic applications in neurology, diabetes and cardiology for approximately $3.5 million in cash. Included in the assets acquired from Biorex are a 500-compound molecular library, as well as the molecules arimoclomol, iroxanadine and bimoclomol, each of which had, at the time of acquisition, successfully completed the European equivalent of a Phase I clinical trial. After management s evaluation of the acquired technology, approximately $3.0 million of the acquisition price was expensed in 2004 as in-process research and development.

As compensation to members of our scientific advisory board and consultants, and in connection with the acquisition of technology, we issue shares of our common stock, stock options and warrants to purchase shares of our common stock. For financial statement purposes, we value these shares of common stock, stock options, and warrants at the fair value of the common stock, stock options or warrants granted, or the services received, whichever is more reliably measurable. We recorded non-cash charges of $0.2 million, $1.4 million, and $2.9 million during 2005, 2004, and 2003, respectively.

In 2006, we expect our research and development expenses to increase primarily as a result of our ongoing Phase II clinical program with arimoclomol and related studies for the treatment of ALS. We estimate that the Phase II trial and related studies will cost approximately $17.8 million, of which approximately $3.8 million had been spent as of December 31, 2005, and will last between 24 to 30 months. Additionally, we estimate that our costs related to the activities of our Massachusetts laboratory will be consistent with expenses incurred in 2005.

General and administrative expense

	Year Ended December 31,		
	2005	**2004**	**2003**
		(In thousands)	
General and administrative expense	$ 6,057	$ 5,924	$ 3,841
Common stock, stock options and warrants issued for general and administrative expense	367	1,977	3,148
	$ 6,424	$ 7,901	$ 6,989

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General and administrative expenses include all administrative salaries and general corporation expenses. Our total general and administrative expenses, including common stock, stock options and warrants issued, were $6.4 million in 2005, $7.9 million in 2004 and $7.0 million in 2003. Our general and administrative expenses, net of common stock, stock options and warrants issued, were $6.1 million in 2005, $5.9 million in 2004 and $3.8 million in 2003. General and administrative expenses during 2005 as compared to 2004 were relatively constant. During 2005 the Company incurred approximately $0.9 million in higher salary expense than 2004, although the difference in total general and administrative expense was substantially smaller between 2005 and 2004 due to one-time expenses associated with our change in auditors in 2004, severance paid to certain members of management in the first half of 2004, and the settlement of certain legal proceedings, for which there was no comparable expenses in 2005. For the same reasons, general and administrative expenses during 2004 were higher as compared to 2003. We expect our general and administrative expenses in 2006 to be slightly higher than those incurred in 2005, as a result of our ongoing Sarbanes-Oxley compliance efforts.

From time to time, we issue shares of our common stock or warrants or options to purchase shares of our common stock to consultants and other service providers in exchange for services. For financial statement purposes, we value these shares of common stock, stock options, and warrants at the fair value of the common stock, stock options or warrants granted, or the services received, whichever is more reliably measurable. We recorded non-cash charges of $0.4 million, $2.0 million, and $3.1 million during 2005, 2004, and 2003, respectively. These charges relate primarily to common stock, stock options and warrants issued in connection with the engagement and retention of financial, business development and scientific advisors. During 2004, as our b2>

Doug Jones

2013
325,000
825,000
229,898
151,038
343,755
1,874,691

Chief Correspondent Lending

2012 300,000 690,706 0 0 244,171 1,234,877

Officer

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(1) The amounts shown in this column represent the total amount of bonus earned by the named executive officers for Fiscal 2013 and Fiscal 2012, whether or not paid in such years.

(2) The amount shown in this column in respect of 2012 represents the full grant date fair value, as determined in accordance with Financial Accounting Standards Board Accounting Standards Codification Topic 718, Compensation Stock Compensation, or FASB ASC TOPIC 718, of $140,353 with respect to 324.14 common units granted to Mr. Kurland by PNMAC on January 1, 2012, which common units were converted into 150,791 Class A Units of PNMAC as part of the recapitalization of PNMAC, and $213,904 with respect to 35.55 preferred units purchased by Mr. Kurland for $35,550 on November 1, 2012, which preferred units were converted into 14,143 Class A Units of PNMAC as part of the recapitalization. PNMAC granted Mr. Kurland such common units, and permitted him to purchase such preferred units, in consideration for his forfeiture of a portion of the common units that were allocated to him under a prior equity incentive plan and issued prior to the completion of our initial public offering. Mr. Kurland forfeited such portion of the common units allocated to him in order to facilitate the participation of certain newly-hired executives in a previous equity incentive plan. The amounts shown in this column in respect of 2013 represent performance-based restricted stock units awarded on June 13, 2013 to Mr. Kurland, Mr. Spector and Mr. Jones in the amounts of 134,570, 50,919 and 19,853, respectively, pursuant to our 2013 Equity Incentive Plan. See " 2013 Outstanding Equity Awards at Fiscal Year-End" below.

(3)

The amounts shown in this column represent the full grant date fair value, as determined in accordance with FASB ASC TOPIC 718, of the nonstatutory stock options awarded on June 13, 2013 to Mr. Kurland, Mr. Spector and Mr. Jones in the amounts of 107,656, 40,735 and 15,882, respectively, pursuant to our 2013 Equity Incentive Plan. See " 2013 Outstanding Equity Awards at Fiscal Year-End" below.

(4)

All Other Compensation for all three named executive officers consists of insurance premiums and gross-up payments for the payment of self-employment taxes by each named executive officer. The Company paid gross-up payments to the named executive officers in the following amounts: $46,361 for Mr. Kurland, $26,833 for Mr. Spector and $10,763 for Mr. Jones during Fiscal 2013 and $20,397 for Mr. Kurland, $13,872 for Mr. Spector and $25,894 for Mr. Jones during Fiscal 2012. PNMAC paid insurance premiums to the named executive officers in the following amounts: $20,255 for Mr. Kurland, $19,654 for Mr. Spector and $10,922 for Mr. Jones during Fiscal 2013 and $23,400 for Mr. Kurland, $23,400 for Mr. Spector and $13,427 for Mr. Jones during Fiscal 2012. PNMAC paid an automobile allowance to the named executive officers in the following amounts during Fiscal 2013: $11,800 for Mr. Kurland and $11,800 for Mr. Spector.

With respect to Mr. Jones, All Other Compensation also includes a $10,200 contribution paid by PNMAC to his 401(k) plan and 13,000 restricted share units awarded by PMT to Mr. Jones for Fiscal 2013 and a $10,000 contribution paid by PNMAC to his 401(k) plan and 15,000 restricted share units awarded by PMT to Mr. Jones in Fiscal 2012, consistent with its compensation program and philosophy, and recorded by PNMAC as a portion of its compensation expense and PCM's management fees.

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In addition, restricted share units were awarded by PMT to Mr. Kurland and Mr. Spector during Fiscal 2013 and Fiscal 2012, consistent with its compensation program and philosophy. The restricted share units were granted on May 14, 2013 and May 16, 2012, and have full grant date fair values, as determined in accordance with FASB ASC TOPIC 718, of $1,679,300 and $1,867,000 for Mr. Kurland, and $1,151,520 and $1,250,890 for Mr. Spector, for Fiscal 2013 and Fiscal 2012, respectively. The restricted share units vest in four equal annual installments beginning on the one-year anniversary of the grant date and entitle each named executive officer to receive dividend equivalents during the vesting period. These full grant date fair values are not included in All Other Compensation for Mr. Kurland and Mr. Spector.

Narrative Disclosure to the 2013 Summary Compensation Table

Employment Agreements

On April 20, 2013, we entered into an employment agreement with Mr. Kurland, pursuant to which he serves as the chairman of our board of directors and Chief Executive Officer and the Chief Executive Officer of PNMAC. On that same date, we also entered into an employment agreement with Mr. Spector, pursuant to which he serves as a member of our board of directors and as our President and Chief Operating Officer and the President and Chief Investment Officer of PNMAC. The terms of these agreements are described below.

The employment agreements, each of which has a three year term, provide Mr. Kurland with an annual base salary of $900,000 and Mr. Spector with an annual base salary of $500,000, in each case, increased annually at a rate determined by our board of directors and Compensation Committee. Mr. Kurland and Mr. Spector are also entitled to receive both cash and equity incentive compensation each year during the term of the employment agreements, awarded at levels determined by our board of directors and Compensation Committee based on annual performance targets.

All equity awards are granted pursuant to our 2013 Equity Incentive Plan and are subject to vesting requirements. Any unvested awards shall immediately vest upon the death or disability of the executive, a termination by us other than for cause (as defined in the employment agreement), a termination by the executive for good reason (as defined in the employment agreement), or the expiration of the term of the employment agreement before any new agreement is reached. All nonstatutory options granted pursuant to our 2013 Equity Incentive Plan are exercisable, subject only to vesting provisions, for a period of ten years from the date of grant, and are eligible for cashless exercise in all circumstances.

All of the compensation and benefits must, at a minimum, be targeted based on performance at a level commensurate with the total compensation paid to the top 25% of executives holding comparable positions in companies of comparable size and sophistication. The agreements also provide for the accrual of twenty days of paid time off at the executive's regular base pay rate during each year of the term, medical benefits, reimbursement for expenses related to tax advice and financial counseling not to exceed $25,000, an automobile allowance of up to $1,500 per month, reimbursement of reasonable business expenses, and participation in such other benefits programs as are provided to our executives generally.

Each of these employment agreements provides for compensation and obligations in the event of certain terminations of employment. Upon a termination due to death or disability, a termination by us without cause, or a termination by the executive for good reason, in addition to any other amounts required by law to be paid to him, the executive would be entitled to the pro rata portion of any bonus earned but unpaid for the year during which the agreement is terminated, and we will generally reimburse the executive or his estate for any amounts paid by him or his estate for coverage of him and his family under our group health medical benefits plan pursuant to the Consolidated Omnibus Budget Reconciliation Act, or COBRA, for as long as the executive or his family is eligible to receive such benefits under COBRA. Upon a termination due to death, the executive's estate will also receive severance payments equal to his base salary for a period of 6 months following such termination. Upon the expiration of the term of the employment agreement or upon a termination by us other than for

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cause or a termination by the executive for good reason, the executive will also serve as a consultant to us for an eighteen-month period commencing on the termination date. During the consulting period, the executive will receive in monthly installments, payments equal to one-twelfth of the executive's median annual base salary and one-twelfth of the executive's median annual incentive compensation, as calculated based on the executive's annual base salary and target incentive compensation for the year in which the termination date occurs and his annual base salary and actual incentive compensation for the two preceding years, provided that such compensation will cease if the executive engages in services for a business that competes with ours.

Each employment agreement also provides that for 18 months following a termination of employment, the executive will not, directly or indirectly, solicit or induce any of our employees, consultants, independent contractors, agents or representatives of the Company, or those of our affiliates, to discontinue employment or engagement with us or our affiliates, or otherwise interfere with those relationships.

Potential Payments Upon Termination or Change in Control

Pursuant to our 2013 Equity Incentive Plan and subject to any contrary provisions in any applicable award agreement, upon the occurrence of a change of control:

all outstanding unvested awards and awards subject to a risk of forfeiture, other than awards conditioned on the achievement of performance goals, will immediately become vested in full and no longer be subject to any risk of forfeiture unless they are assumed or otherwise continued in a manner satisfactory to the Committee, or substantially equivalent rights are provided in substitution for such awards, in each case by the acquiring or succeeding entity or one of its affiliates; and

if a pro rata portion of the performance goals under awards conditioned on the achievement of performance goals or other business objectives has been achieved as of the effective date of the change of control, then such performance goals or other business objectives shall be deemed satisfied as of such change of control with respect to a pro rata portion of the number of shares subject to the original award. The pro rata portion of the performance goals or other business objectives and the number of shares subject to the original awards shall each be based on the length of time within the performance period which has elapsed prior to the change of control. The pro rata portion of any award deemed earned in this manner will be paid out within 30 days following the change of control. The remaining portion of such an award that is not eligible to be deemed earned as of the change of control will be deemed to have been satisfied, earned, or forfeited as of the change of control in such amounts as the Committee shall determine in its sole discretion unless that remaining portion is assumed by the acquiring or succeeding entity or one of its affiliates, which will be deemed to occur if that remaining portion is subjected to (i) comparable performance goals based on the post-change of control business of the acquiror or succeeding entity or one if its affiliates, and (ii) a measurement period using a comparable period of time to the original award, each in a manner satisfactory to the Committee.

A change of control is defined as the occurrence of any of the following: (1) a transaction, as described above, unless securities possessing more than 50% of the total combined voting power of the resulting entity or ultimate parent entity are held by one or more persons who held securities possessing more than 50% of the total combined voting power of our Company immediately prior to the transaction; (2) any person or group of persons, excluding us and certain other related entities, directly or indirectly acquires beneficial ownership of securities possessing more than 20% of the total combined voting power of our Company, unless pursuant to a tender or exchange offer that our board of directors recommends stockholders accept; (3) over a period of no more than 36 consecutive months there is a change in the composition of our board of directors such that a majority of our directors

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ceases to be composed of individuals who either (i) have been directors continuously since the beginning of that period, or (ii) have been elected or nominated for election as members of our board of directors during such period by at least a majority of the remaining members of our board of directors who have been directors continuously since the beginning of that period; or (4) a majority of the members of our board of directors vote in favor of a decision that a change of control has occurred.

Summary of Equity Award Agreements

During Fiscal 2013, our named executive officers were awarded non-statutory stock options. The form of stock option award agreement provides for the award of stock options to purchase the optioned shares. In general, and except as otherwise provided by the Compensation Committee, one-third (1/3) of the optioned shares will vest in a lump sum on each of the first, second, and third anniversaries of the vesting commencement date, subject to the recipient's continued service through each anniversary, and each stock option will have a term of ten years from the date of grant. Additionally, the stock options expire (1) immediately upon termination of the holder's employment or other association with us for cause, (2) one year after the holder's employment or other association is terminated due to death or disability and (3) three months after the holder's employment or other association is terminated for any other reason.

During Fiscal 2013, our named executive officers also were awarded performance-based restricted stock units, or RSUs. The forms of RSU award agreement referred to herein provide for the award of performance-based RSUs to obtain, for each RSU, a variable number of shares of our Class A common stock and time-based RSUs to obtain, for each RSU, one share of our Class A common stock. One-third of all time-based RSUs vest in a lump sum on each of the first, second, and third anniversaries of the vesting commencement date, subject to the recipient's continued service through each anniversary. The number of shares received upon vesting of performance-based RSUs is determined based on the attainment of the performance goals, subject to conditions including continued employment throughout the performance period.

2013 Outstanding Equity Awards at Fiscal Year-End

The following table provides information about outstanding equity awards of our named executive officers as of the end of Fiscal 2013:

	Option Awards(1)					Stock Awards	
Name	Grant Date	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price ($/sh)	Option Expiration Date	Number of Shares or Units of Stock Granted That Have Not Vested (#)	Market Value of Shares or Units of Stock Granted That Have Not Vested(2)
Stanford L. Kurland	06/13/2013		107,656	21.03	06/12/2023	134,570	1,558,321
David A. Spector	06/13/2013		40,735	21.03	06/12/2023	50,919	589,642
Doug Jones	06/13/2013		15,882	21.03	06/12/2023	19,853	229,898

(1) One-third (1/3) of the optioned shares will vest in a lump sum on each of the first, second, and third anniversaries of the vesting commencement date, subject to the recipient's continued service through each anniversary.

(2) Per share grant date fair value of stock awards is $11.58.

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401(k) Plan

PNMAC maintains a tax-qualified 401(k) retirement plan for all employees who satisfy certain eligibility requirements. Under our 401(k) plan, employees may elect to defer a portion of their eligible compensation subject to applicable annual Code limits. Under the 401(k) plan, PNMAC makes matching contributions to participants equal to 100% of the participant's elective deferrals, up to a maximum of 4% of the participant's annual compensation. We intend for the 401(k) plan to qualify under Section 401(a) and 501(a) of the Code so that contributions by employees to the 401(k) plan, and income earned on those contributions, are not taxable to employees until withdrawn from the 401(k) plan.

Compensation Committee Interlocks and Insider Participation

None of the members of our Compensation Committee is or has at any time during the past year been one of our officers or employees. None of our executive officers currently serves or in the past year has served as a member of the board of directors or compensation committee of any entity that has one or more executive officers serving on our board of directors or compensation committee.

Compensation Risks

We believe that any risks arising from our compensation policies and practices are not reasonably likely to have a material adverse effect on the Company. In addition to cash compensation that is paid to officers and employees of our wholly-owned subsidiary, PNMAC, we also use long-term incentive compensation in the form of equity-based awards, which we issue under our 2013 Equity Incentive Plan. The long-term incentive compensation awards are designed to align the interests of our officers and service providers with those of our stockholders, all of whom will share together in the creation of value through capital appreciation. We believe that equity-based awards are consistent with our stockholders' interest in book value growth as these individuals will be less incentivized to take short-term risk and more incentivized to grow book value for stockholders over time.

Non-Employee Director Compensation

The following table summarizes the annual retainer fees paid to our non-employee directors during Fiscal 2013:

Base Annual Retainer, all board members	$ 65,000
Base Annual Retainer, all committee members:	
Audit Committee	$ 7,750
Compensation Committee	$ 7,750
Governance and Nominating Committee	$ 5,750
Related-Party Matters Committee	$ 5,750
Finance Committee	$ 7,750
Additional Annual Retainer, all committee chairs:	
Audit Committee	$ 10,750
Compensation Committee	$ 10,750
Governance and Nominating Committee	$ 7,750
Related-Party Matters Committee	$ 7,750
Finance Committee	$ 10,750

In addition, our directors are eligible to receive certain types of equity-based awards under our 2013 Equity Incentive Plan. Each independent director newly elected or appointed to our board of directors is entitled to receive a one-time equity grant of approximately $87,000 in RSUs. Prior to the vesting of an RSU, such RSU is generally subject to forfeiture upon termination of service to us.

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During Fiscal 2013, each of Messrs. Botein, Hunt, Mazzella, Nanji, Taylor and Wiedman received a grant of 4,459 time-based RSUs which vest ratably over a three (3) year period beginning on the one (1) year anniversary of the date of the grant, May 14, 2013, subject to continued service through each vesting date. Upon her appointment to our board of directors, Ms. Youssouf received a grant of 2,614 RSUs, which vest ratably over a three (3) year period beginning on the one (1) year anniversary of the date of the grant, November 14, 2013, subject to continued service through each vesting date.

Upon a change of control (as defined in our 2013 Equity Incentive Plan), all outstanding equity awards granted to non-employee directors will be assumed, or substantially equivalent rights will be substituted, or the awards otherwise will be continued in a manner satisfactory to the Compensation Committee, by the acquiring or succeeding entity or its affiliate.

2013 Director Compensation Table*

The table below summarizes the compensation earned by each non-employee director who served on the board of directors for Fiscal 2013.

Name(1)	Fees Earned or Paid in Cash ($)(2)	Stock Awards ($)(3)	Total ($)
Matthew Botein	64,187	86,995	151,182
James K. Hunt	60,945	86,995	147,940
Joseph Mazzella	54,625	86,995	141,620
Farhad Nanji	64,187	86,995	151,182
John Taylor	57,866	86,995	144,861
Mark Wiedman	49,599	86,995	136,594
Emily Youssouf	9,036	43,131	52,167(4)

* The columns for "Option Awards," "Non-Equity Incentive Plan Compensation," "Change in Pension Value," "Nonqualified Deferred Compensation Earnings" and "All Other Compensation" have been omitted because they are not applicable.

(1) Mr. Kurland, our chairman of the board and Chief Executive Officer, and Mr. Spector, a director and our President and Chief Operating Officer, are not included in this table as they are officers of the Company and thus receive no compensation for their services as directors. Messrs. Kurland and Spector received compensation as officers of the Company for Fiscal 2013 as shown in the "2013 Summary Compensation Table."

(2) Reflects fees earned by the director in Fiscal 2013, whether or not paid in such year.

(3) Reflects the full grant date fair value, as determined in accordance with FASB ASC TOPIC 718, of RSUs granted to Messrs. Botein, Hunt, Nanji, Mazzella, Taylor and Wiedman on May 14, 2013 and Ms. Youssouf on November 14, 2013. For more information on the assumptions used in our estimates of value, please refer to *Note 22 Stock-based Compensation* in our Annual Report on Form 10-K filed on March 14, 2014. As of December 31, 2013, each of our directors held an aggregate number of RSUs in the following amounts: Messrs. Botein, Hunt, Mazzella, Nanji, Taylor and Wiedman 4,459 and Ms. Youssouf 2,614.

(4) Reflects a pro rata portion of the annual fees described above for the portion of 2013 for which Ms. Youssouf was a director. Ms. Youssouf joined our board of directors on November 14, 2013.

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PRINCIPAL STOCKHOLDERS

The following table sets forth information regarding the beneficial ownership of shares of Class A common stock by (1) each person known to us to beneficially own more than 5% of the outstanding shares of Class A common stock, (2) each of our directors and named executive officers and (3) all of our directors and executive officers as a group.

Beneficial ownership reflected in the table below is based on 20,879,486 shares of Class A common stock outstanding as of March 12, 2014, and, with respect to any individual, includes the total shares of Class A common stock beneficially owned by such individual and his or her personal financial planning vehicles. Beneficial ownership is determined with respect to each stockholder in accordance with the rules of the SEC by assuming that such stockholder (and no other stockholder) has exchanged all of its or his Class A Units of PNMAC for an equivalent number of shares of our Class A common stock.

Except as otherwise indicated below, the address for each person or entity listed in the table is c/o PennyMac Financial Services, Inc., 6101 Condor Drive, Moorpark, California 93021.

	Class A Common Stock Beneficially Owned(1)		
Beneficial Owner	**Number**	**Percent**	**% of Total Voting Power and Total Economic Interest in PNMAC(2)**
5% Stockholders			
BlackRock Mortgage Ventures, LLC(3) 40 East 52nd Street New York, New York 10022	16,073,278	45.72%	21.18%
HC Partners LLC(4) 200 Clarendon Street, 59th Floor Boston, Massachusetts 02116	20,169,732	49.14%	26.58%
Fidelity Investments Charitable Gift Fund(5) 200 Seaport Boulevard, Z3B Boston, Massachusetts 02210	6,110,000	29.26%	8.05%
Entities affiliated with Leon G Cooperman(6) 90 Park Avenue, 40th Floor New York, New York 10016	2,759,600	11.67%	3.64%
Entities affiliated with Bridger Management, LLC(7) 90 Park Avenue, 40th Floor New York, New York 10016	1,725,000	7.63%	2.27%
Kurland Family Investments, LLC(8)	8,314,990	28.48%	10.96%
Directors and Named Executive Officers			
Stanford L. Kurland(9)	8,599,338	29.17%	11.33%
David A. Spector(10)	1,699,729	7.53%	2.24%
Doug Jones(11)	793,767	3.66%	1.05%
Matthew Botein(12)	1,218,552	5.51%	1.61%
James K. Hunt	4,000	*	*
Joseph Mazzella(13)	331,052	1.56%	*
Farhad Nanji(14)	134,569	*	*
John Taylor		*	*
Mark Wiedman(15)	54,556	*	*
Emily Youssouf		*	*
Directors and executive officers as a group (17 persons)	18,044,973	72.40%	23.78%

*

Represents less than 1.0%.

(1)

Subject to the terms of the exchange agreement, Class A Units of PNMAC not held by us are exchangeable at any time and from time to time for shares of our Class A common stock on a one-for-one basis, subject to customary conversion rate

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adjustments for stock splits, stock dividends, reclassifications and certain other transactions that would cause the number of outstanding shares of Class A common stock to be different than the number of Class A Units of PNMAC owned by PennyMac Financial Services, Inc. The number of shares of Class A common stock listed in this table as being beneficially owned as a result of Class A Units of PNMAC held by any entity or individual assumes an exchange of such Class A Units for shares of Class A common stock on a one-for-one basis.

(2)

Represents the percentage of voting power of the Class A common stock and Class B common stock of PennyMac Financial Services, Inc. voting together as a single class. Each holder of Class A Units of PNMAC other than us also holds one share of our Class B common stock. The shares of Class B common stock have no economic rights but entitle the holder, without regard to the number of shares of Class B common stock held, to a number of votes on matters presented to our stockholders that is equal to the aggregate number of Class A Units of PNMAC held by such holder. As a holder exchanges Class A Units of PNMAC for shares of our Class A common stock pursuant to the exchange agreement, the voting power afforded to the holder by its share of Class B common stock will be automatically and correspondingly reduced. Total economic interest in PNMAC is calculated as the percentage of all outstanding Class A Units of PNMAC beneficially held by the stockholder, directly or indirectly through PennyMac Financial Services, Inc., assuming that each share of Class A common stock held is equivalent to one Class A Unit of PNMAC.

(3)

Consists entirely of 512,631 shares of Class A common stock acquired in its role as an investment adviser for certain client accounts, 1,800,000 shares of Class A Common Stock received upon exchange of its Class A Units of PNMAC on December 13, 2013, and 13,760,647 Class A Units of PNMAC exchangeable for shares of Class A common stock. BlackRock Mortgage Ventures, LLC is indirectly wholly-owned by BlackRock, Inc. BlackRock, Inc. controls the voting and investment power with respect to the securities held by BlackRock Mortgage Ventures, LLC and, therefore, may be deemed to be the beneficial owner of the shares of Class A common stock beneficially owned by that entity.

(4)

Consists entirely of 20,169,732 Class A Units of PNMAC exchangeable for shares of Class A common stock.

(5)

As reported in a Schedule 13D filed with the SEC on October 11, 2013 by Fidelity Investments Charitable Gift Fund. In the Schedule 13D, Fidelity Investments Charitable Gift Fund does not affirm the existence of a group and discloses that it has sole voting and dispositive power as to 6,110,000 shares.

(6)

Consists of 913,000 shares of Class A common stock held in managed accounts over which Leon Cooperman has investment discretion and 1,846,600 shares of Class A common stock held in the accounts of private investment entities over which Leon Cooperman has investment discretion. Mr. Cooperman has sole voting and dispositive power over 1,846,600 shares of Class A common stock and shared voting and dispositive power over 913,000 shares of Class A common stock. Mr. Cooperman is the Managing Member of Omega Associates, L.L.C. ("Associates"). Associates is a private investment firm formed to invest in and act as general partner of investment partnerships or similar investment vehicles. Associates is the general partner of limited partnerships known as Omega Capital Partners, L.P. ("Capital LP"), Omega Capital Investors, L.P.("Investors LP"), and Omega Equity Investors, L.P. ("Equity LP"). These entities are private investment firms engaged in the purchase and sale of securities for investment for their own accounts. Mr. Cooperman is the President and majority stockholder of Omega Advisors, Inc. ("Advisors"), engaged in providing investment management services. Advisors serves as the investment manager to Omega Overseas Partners, Ltd. ("Overseas"). Mr. Cooperman has investment discretion over portfolio investments of Overseas. Advisors also serves as a discretionary investment advisor to a limited number of institutional clients (the "Managed Accounts"). As to the shares owned by the Managed Accounts, there would be shared power to dispose or to direct the disposition of such shares because the owners of the Managed Accounts may be deemed beneficial owners of such shares pursuant to Rule 13d-3 under the Act as a result of their right to terminate the discretionary account within a period of 60 days. Mr. Cooperman is the ultimate controlling person of Associates, Capital LP, Investors LP, Equity LP, and Advisors. Capital LP holds 652,500 shares of Class A common stock; Investors LP holds 198,400 shares of Class A common stock; Equity LP holds 286,600 shares of Class A common stock; Overseas holds 709,100 shares of Class A common stock; and the Managed Accounts hold 913,000 shares of Class A common stock. This information is as reported in the Schedule 13D jointly filed on May 20, 2013 by Leon G. Cooperman and Omega Capital Partners LP.

(7)

Consists of shares of Class A common stock held of record by Swiftcurrent Partners L.P. and 1,041,880 shares of Class A common stock held of record by Swiftcurrent Offshore Master, Ltd. Bridger Management LLC is the investment adviser to each of these entities and Roberto Mignone is the managing member of Bridger Management, LLC. and, as such, each of them have shared voting and dispositive power over these shares. This information is as reported in Amendment No. 2 to Schedule 13G jointly filed January 2, 2014 by the foregoing entities.

(8)

Consists entirely of 8,314,990 Class A Units of PNMAC exchangeable for shares of Class A common stock. Stanford L. Kurland, as the sole manager of Kurland Family Investments, LLC, controls the voting and investment power with respect to the securities held by that entity and, therefore, may be deemed to be the beneficial owner of the shares of Class A common stock beneficially owned by that entity.

(9)

Consists entirely of 8,599,338 Class A Units of PNMAC exchangeable for shares of Class A common stock, including 8,314,990 Class A Units of PNMAC owned by Kurland Family Investments, LLC.

(10)

Consists entirely of 1,699,729 Class A Units of PNMAC exchangeable for Class A common stock, including 465,604 Class A Units of PNMAC owned by ST Family Investment Company LLC.

(11) Consists entirely of 793,767 Class A Units of PNMAC exchangeable for shares of Class A common stock.

(12) Includes 1,218,552 Class A Units of PNMAC exchangeable for shares of Class A common stock.

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(13) Includes 331,052 Class A Units of PNMAC exchangeable for shares of Class A common stock. Does not include 407,031 Class A Units of PNMAC owned by the Mazzella Family Irrevocable Trust. Mr. Mazzella is not a trustee of that entity and, therefore, would not be deemed to be the beneficial owner of the Class A Units of PNMAC held by that entity.

(14) Includes 122,109 Class A Units of PNMAC exchangeable for shares of Class A common stock.

(15) Consists entirely of 54,556 Class A Units of PNMAC exchangeable for shares of Class A common stock.

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CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

Other than compensation arrangements, we describe below transactions and series of similar transactions, during our last three fiscal years, to which we were a party or will be a party, in which:

- the amounts involved exceeded or will exceed $120,000; and
- any of the directors, executive officers or holders of more than 5% of the membership interests of PNMAC, or any member of the immediate family of the foregoing persons, had or will have a direct or indirect material interest.

Compensation arrangements for our directors and named executive officers are described elsewhere in this Report.

Exchange Agreement

We have entered into an exchange agreement with all of the owners of Class A Units of PNMAC other than us that entitles those owners to exchange their Class A Units of PNMAC for shares of our Class A common stock on a one-for-one basis, subject to customary conversion rate adjustments for stock splits, stock dividends, reclassifications and certain other transactions that would cause the number of outstanding shares of Class A common stock to be different than the number of Class A Units of PNMAC owned by PennyMac Financial Services, Inc. Those owners are able to exercise their exchange rights at any time. In addition, we can require those owners to exercise their exchange rights (i) in connection with a change of control of our Company or (ii) if no holder of Class A Units of PNMAC (other than us) holds 3% or more of all Class A Units of PNMAC, in each case unless the cash and, in the case of a change of control, marketable securities that they would receive in connection with such exchange (including the after-tax value of amounts received pursuant to the tax receivable agreement and any amounts advanced to them by us, which advanced amounts will be repaid upon the sale of the Class A common stock received in the exchange) would not be sufficient to cover the taxes that those owners would become liable for as a result of such exchange. Even if that cash would not be sufficient to cover their taxes, we can still require those owners to exchange if no holder holds more than 3% of all Class A Units of PNMAC by electing to effect the exchange at 110% of the exchange rate otherwise in effect. We can also require an owner who is an officer or employee to exercise his or her exchange rights, upon the termination of his or her employment. If we have distributed excess cash or property to our stockholders prior to an exchange of Class A Units of PNMAC by an owner pursuant to the exchange agreement, then upon such exchange such owner will also receive, in respect of each share of Class A common stock issued in such exchange, the amount of such excess cash or property that was distributed in each such prior distribution in respect of each share of Class A common stock outstanding at the time of such prior distribution. Excess property consists of any property, other than cash, that was not distributed to PennyMac Financial Services, Inc. by PNMAC. Excess cash consists of any amount by which the cumulative amount of all cash distributed by us to our stockholders exceeds (i) the cumulative amount of all cash distributed to us by PNMAC, LLC, less (ii) the cumulative amount of all cash payments made by us for any purpose other than repaying debt or making distributions to our stockholders, each measured as of the time of the exchange of Class A Units of PNMAC. The exchange agreement provides, however, that voluntary exchanges must be for the lesser of a stated minimum number of Class A Units of PNMAC or all of the vested Class A Units of PNMAC held by such owner. The exchange agreement also provides that an owner will not have the right to exchange Class A Units of PNMAC if we determine that such exchange would be prohibited by law or regulation or would violate other agreements with PNMAC to which the owner may be subject. We may impose additional restrictions on exchanges that we determine to be necessary or advisable so that PNMAC is not treated as a "publicly traded partnership" for United States federal income tax purposes.

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Stockholder Agreements

We have entered into separate stockholder agreements with BlackRock and Highfields which provide that our board of directors will consist of no more than nine directors as long as those entities and their affiliates hold at least 10% of the voting power of our outstanding shares of capital stock. Those agreements also provide that each of BlackRock and Highfields will have the right to nominate two individuals for election to our board of directors as long it, together with its affiliates, holds at least 15% of the voting power of our outstanding shares of capital stock, and the right to nominate one individual for election to our board of directors as long as it, together with its affiliates, holds at least 10% of the voting power of our outstanding shares of capital stock. We, in turn, are obligated to use our best efforts to ensure that these nominees are elected. In addition, those agreements provide that each of BlackRock and Highfields, as long as it, together with its affiliates, holds at least 10% of the voting power of our outstanding shares of capital stock, will have the right to nominate one member of each committee of our board of directors. As long as those nominees meet the independence standards applicable to those committees, we will appoint them as members of those committees. Those agreements also provide that neither our certificate of incorporation nor our bylaws, as in effect from time to time, may be amended in any manner that is adverse to BlackRock, Highfields or their respective affiliates without the consent of BlackRock or Highfields, as applicable, as long it, together with its affiliates, holds at least 5% of the voting power of our outstanding shares of capital stock.

Registration Rights Agreement

We have entered into a registration rights agreement with BlackRock, Highfields and the other owners of PNMAC other than PennyMac Financial Services, Inc. pursuant to which BlackRock, Highfields and certain permitted transferees have the right, under certain circumstances and subject to certain restrictions, to require us to register for resale the shares of our Class A common stock delivered in exchange for Class A Units of PNMAC held by them. In October 2013, we filed a registration statement to register for resale the shares of our Class A common stock delivered in exchange for Class A Units of PNMAC on behalf of BlackRock, Highfields and other selling stockholders. The registration statement was declared effective on October 29, 2013. All securities registered under this registration statement are available for sale in the open market unless restrictions apply.

Demand Registration Rights. BlackRock and Highfields and certain permitted transferees each have the right to demand that we register their Class A common stock for resale, subject to the conditions set forth in the registration rights agreement, no more than three times in any twelve month period. BlackRock and Highfields and certain permitted transferees have the right under the registration rights agreement to require that we register their Class A common stock for resale. Such registration demand must reasonably be expected to result in aggregate gross cash proceeds to such demanding stockholder in excess of $25 million. Each of BlackRock and Highfields and certain permitted transferees will have the right to participate in any such demand registrations. We will not be obligated to effect a demand registration within 120 days of the effective date of a registration statement filed by us. We may postpone the filing of a registration statement for up to 60 days once in any 12-month period if our board of directors determines in good faith that the filing would reasonably be expected to materially adversely affect any material financing or acquisition of ours or require premature disclosure of information that would reasonably be expected to be materially adverse to us. The underwriters of any underwritten offering have the right to limit the number of shares to be included in a registration statement filed in response to the exercise of these demand registration rights. We must pay all expenses, except for underwriters' discounts and commissions, incurred in connection with these demand registration rights.

Piggyback Registration Rights. BlackRock, Highfields, certain of their permitted transferees and the minority stockholders which are parties to the agreement will each have the right to "piggyback" on

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any registration statements that we file on an unlimited basis, subject to the conditions set forth in the registration rights agreement. If we register any securities for public sale, stockholders with piggyback registration rights under the registration rights agreement have the right to include their shares in the registration for resale by them, subject to specified limitations and exceptions.

S-3 Registration Rights. If we are eligible to file a registration statement on Form S-3, the stockholders with S-3 registration rights under the registration rights agreement and certain permitted transferees can request that we register their shares for resale. Any registration must be reasonably expected by the demanding stockholder to result in aggregate gross cash proceeds to such demanding stockholder in excess of $10 million, and no more than three demands for an S-3 registration may be made in any 12-month period. If we are eligible as a Well Known Seasoned Issuer, or WKSI, the requesting stockholders may request that the shelf registration statement utilize the automatic shelf registration process under Rule 415 and Rule 462 promulgated under the Securities Act. If we are not eligible as a WKSI or are otherwise ineligible to utilize the automatic shelf registration process, then we are required to use our reasonable efforts to have the shelf registration statement declared effective.

Tax Receivable Agreement

As described above, the holders of Class A Units of PNMAC other than us may (subject to the terms of the exchange agreement) exchange their Class A Units of PNMAC for shares of our Class A common stock, initially on a one-for-one basis. PNMAC intends to have in effect an election under Section 754 of the Code effective for each taxable year in which an exchange of Class A Units of PNMAC for shares of Class A common stock occurs, which may result in a special adjustment for PennyMac Financial Services, Inc. with respect to the tax basis of the assets of PNMAC at the time of an exchange of Class A Units of PNMAC, which adjustment affects only us, which we refer to as the "corporate taxpayer." The subsequent exchanges are expected to result in special increases for the corporate taxpayer in the tax basis of the assets of PNMAC that otherwise would not have been available. These increases in tax basis may reduce the amount of tax that the corporate taxpayer would otherwise be required to pay in the future. These increases in tax basis may also decrease gains (or increase losses) on future dispositions of certain capital assets to the extent tax basis is allocated to those capital assets. The IRS may challenge all or part of the existing tax basis, tax basis increase and increased deductions, and a court could sustain such a challenge.

We have entered into a tax receivable agreement with the owners of PNMAC other than us that provides for the payment from time to time by the corporate taxpayer to those owners of 85% of the amount of the net tax benefits, if any, that the corporate taxpayer is deemed to realize under certain circumstances as a result of (i) increases in tax basis resulting from exchanges of Class A Units of PNMAC and (ii) certain other tax benefits related to our entering into the tax receivable agreement, including tax benefits attributable to payments under the tax receivable agreement. These payment obligations are obligations of the corporate taxpayer and not of PNMAC. For purposes of the tax receivable agreement, the tax benefit deemed realized by the corporate taxpayer will be computed by comparing the actual income tax liability of the corporate taxpayer (calculated with certain assumptions) to the taxes that the corporate taxpayer would have been required to pay had there been no increase to the tax basis of the assets of PNMAC as a result of the exchanges, and had the corporate taxpayer not entered into the tax receivable agreement. The term of the tax receivable agreement will continue until all such tax benefits have been utilized or expired, unless we exercise our right to terminate the tax receivable agreement. In the event of termination of the tax receivable agreement, we would be required to make an immediate payment equal to the present value of the anticipated future net tax benefits, which upfront payment may be made years in advance of the actual realization of such future benefits. Estimating the amount of payments that may be made under the tax receivable agreement is by its nature imprecise, insofar as the calculation of amounts payable depends

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on a variety of factors. The actual increase in tax basis, as well as the amount and timing of any payments under the tax receivable agreement, will vary depending upon a number of factors, including:

- the timing of exchanges — for instance, the increase in any tax deductions will vary depending on the fair value, which may fluctuate over time, of the depreciable or amortizable assets of PNMAC at the time of each exchange;

- the price of shares of our Class A common stock at the time of the exchange — the tax basis increase in assets of PNMAC for the corporate taxpayer, as well as any related increase in allocations of tax deductions to the corporate taxpayer, is directly proportional to the price of shares of our Class A common stock at the time of the exchange;

- the extent to which such exchanges are taxable — if an exchange is not taxable for any reason, increased deductions will not be available; and

- the amount and timing of our income — the corporate taxpayer will be required to pay 85% of the net tax benefits as and when those benefits are treated as realized under the terms of the tax receivable agreement. If the corporate taxpayer does not have taxable income, the corporate taxpayer generally is not required (absent a change of control or circumstances requiring an early termination payment) to make payments under the tax receivable agreement for that taxable year because no benefit will have been actually realized. However, any tax benefits that do not result in realized benefits in a given tax year will likely generate tax attributes that may be utilized to generate benefits in previous or future tax years. The utilization of such tax attributes will result in payments under the tax receivable agreement.

We expect that the payments that we may make under the tax receivable agreement will be substantial. There may be a material negative effect on our liquidity if, as a result of timing discrepancies or otherwise, the payments under the tax receivable agreement exceed the actual benefits we realize in respect of the tax attributes subject to the tax receivable agreement and/or distributions to us by PNMAC are not sufficient to permit us to make payments under the tax receivable agreement after we have paid taxes. Furthermore, our obligations to make payments under the tax receivable agreement could make us a less attractive target for an acquisition, particularly in the case of an acquirer that cannot use some or all of the tax benefits that are deemed realized under the tax receivable agreement. The payments under the tax receivable agreement are not conditioned upon the continued ownership of us by the exchanging owners of PNMAC.

In addition, the tax receivable agreement provides that upon certain mergers, asset sales, other forms of business combinations or other changes of control, the corporate taxpayer's (or its successor's) obligations with respect to exchanged or acquired Class A Units of PNMAC (whether exchanged or acquired before or after such transaction) would be based on certain assumptions, including that the corporate taxpayer would have sufficient taxable income to fully utilize the deductions arising from the increased tax deductions and tax basis and other benefits related to entering into the tax receivable agreement. As a result, (i) we could be required to make payments under the tax receivable agreement that are greater than or less than the specified percentage of the actual net tax benefits we realize in respect of the tax attributes subject to the tax receivable agreement and (ii) if we elect to terminate the tax receivable agreement early, we would be required to make an immediate payment equal to the present value of the anticipated future net tax benefits, which upfront payment may be made years in advance of the actual realization of such future benefits. In these situations, our obligations under the tax receivable agreement could have a substantial negative impact on our liquidity, as well as our attractiveness as a target for an acquisition.

Decisions made by certain owners of Class A Units of PNMAC in the course of running our business, such as with respect to mergers, asset sales, other forms of business combinations or other changes in control, may influence the timing and amount of payments that are received by an

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exchanging or selling owner under the tax receivable agreement. For example, the earlier disposition of assets following an exchange or acquisition transaction will generally accelerate payments under the tax receivable agreement and increase the present value of such payments.

Payments are generally due under the tax receivable agreement within a specified period of time following the filing of our tax return for the taxable year with respect to which the payment obligation arises, although interest on such payments will begin to accrue at a rate of LIBOR plus 100 basis points from the due date (without extensions) of such tax return. Payments not made when due under the tax receivable agreement generally would accrue interest at a rate of LIBOR plus 500 basis points. However, in the event that we do not have sufficient cash available to make a payment under the tax receivable agreement when that payment is due, under certain circumstances we may elect to defer that payment for up to two years. Payments that are deferred pursuant to this election would accrue interest at a rate of LIBOR plus 350 basis points.

Payments under the tax receivable agreement will be based on the tax reporting positions that we will determine. Although we are not aware of any issue that would cause the IRS to challenge a tax basis increase, the corporate taxpayer will not be reimbursed for any payments previously made under the tax receivable agreement (except to the extent such amounts can be applied against future amounts that would otherwise be due under the tax receivable agreement). As a result, in certain circumstances, payments could be made under the tax receivable agreement in excess of the benefits that the corporate taxpayer actually realizes in respect of the tax attributes subject to the tax receivable agreement.

PNMAC Limited Liability Company Agreement

We are the sole managing member of PNMAC. Accordingly, we operate and control all of the business and affairs of PNMAC and, through PNMAC and its operating entity subsidiaries, conduct our business.

Pursuant to the limited liability company agreement of PNMAC, we have the right to determine when distributions will be made to unit holders of PNMAC and the amount of any such distributions, other than with respect to tax distributions as described below. If a distribution is authorized; such distribution will be made to the unit holders of PNMAC pro rata in accordance with the percentages of their respective limited liability company interests.

The unit holders of PNMAC, including us, will incur U.S. federal, state and local income taxes on their proportionate share of any taxable income of PNMAC. Except as otherwise required under Section 704(c) of the Code, net profits and net losses of PNMAC will generally be allocated to its unit holders (including us) pro rata in accordance with their respective limited liability company interests. The limited liability company agreement of PNMAC will provide for quarterly cash distributions, which we refer to as "tax distributions," to the holders of the Class A Units of PNMAC if we, as the sole managing member of PNMAC, determine that the taxable income of PNMAC gives rise to taxable income for such holders. Generally, these quarterly tax distributions will be computed based on the taxable income of PNMAC multiplied by an assumed tax rate determined by us. Tax distributions will be made only to the extent that all distributions from PNMAC for the relevant year were insufficient to cover such tax liabilities.

The limited liability company agreement of PNMAC also provides that substantially all expenses incurred by or attributable to us (such as expenses incurred in connection with this offering), but not including our obligations incurred under the tax receivable agreement and our income tax expenses, will be borne by PNMAC.

The limited liability company agreement of PNMAC generally provides that at any time we issue a share of our Class A common stock or any other equity security, the net proceeds we receive with

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respect to such share, if any, shall be concurrently transferred to PNMAC and PNMAC will issue to us one Class A Unit with respect to such issuance of Class A common stock (or another equity interest in PNMAC with respect to other equity issuances by us). Conversely, if at any time, any shares of our Class A common stock are redeemed by us for cash, then PNMAC will redeem from us the same number of Class A Units of PNMAC (subject to any change in the initial exchange rate provided for in the exchange agreement) at the same price.

Other than us, in our capacity as managing member, holders of the Class A Units of PNMAC will have no voting rights with respect to PNMAC, except that (i) the managing member shall not create additional classes of units or securities for issuance to any party other than us and (ii) the managing member and PNMAC shall take no action or enter into any agreement that would limit the ability of PNMAC to make tax distributions or the ability of the managing member to make payments under the tax receivable agreement, provided that the managing member and PNMAC may enter into credit, financing or warehousing or similar agreements that limit or prohibit the making of tax distributions or payments under the tax receivable agreement if there is a default or event of default or if such distributions could result in a default or event of default thereunder, in each case without the consent of each of BlackRock and Highfields, as long as it, together with its affiliates, holds any Class A Units of PNMAC.