CYTRX CORP
Form S-3/A
July 29, 2003
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As filed with the Securities and Exchange Commission on July 29, 2003

Reg. No. 333-106629

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

AMENDMENT NO. 1

TO

FORM S-3

REGISTRATION STATEMENT

UNDER

THE SECURITIES ACT OF 1933

CYTRX CORPORATION

(Exact name of registrant as specified in its charter)

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

CytRx Corporation

11726 San Vicente Boulevard, Suite 650

Los Angeles, California 90049

(Address, including zip code, and telephone number, including area code, of Registrant s principal executive offices)

Steven A. Kriegsman

CytRx Corporation

11726 San Vicente Boulevard., Suite 650

Los Angeles, California 90049

(310) 826-5648

(Name, address, including zip code, and telephone number, including area code, of agent for service)

With a copy to:

Sanford J. Hillsberg, Esq.

Istvan Benko, Esq.

Troy & Gould Professional Corporation

1801 Century Park East, Suite 1600, Los Angeles, California 90067

(310) 553-4441

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

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

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

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

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

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

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount to be Registered	Proposed Maximum Offering Price Per Share	Proposed Maximum Aggregate Offering Price	Amount of Registration Fee
Common Stock, $.001 par value	5,168,898 shares	$ 2.175(1)	$ 11,242,353	$ 909.51
Common Stock, $.001 par value	200,000 shares(2)	$ 1.00(3)	$ 200,000	$ 16.18
Common Stock, $.001 par value	900,000 shares(2)	$ 0.20(3)	$ 180,000	$ 14.58
Common Stock, $.001 par value	372,804 shares(2)	$ 1.85(3)	$ 689,687	$ 55.80
Common Stock, $.001 par value	808,651 shares(2)	$ 3.05(3)	$ 2,466,386	$ 199.53
Common Stock, $.001 par value	100,000 shares(2)	$ 0.75(3)	$ 75,000	$ 6.07
Common Stock, $.001 par value	100,000 shares(2)	$ 0.90(3)	$ 90,000	$ 7.29
Common Stock, $.001 par value	200,000 shares(2)	$ 1.05(3)	$ 210,000	$ 16.99
Common Stock, $.001 par value	82,500 shares(2)	$ 2.00(3)	$ 165,000	$ 13.35
Warrants	735,136 warrants(4)			(4)
Total Registration Fee				$ 1,239.30(5)

(1) Estimated solely for the purpose of calculating the registration fee. Based, pursuant to Rule 457, on the average of the high and low sale prices of Registrant s Common Stock as reported on Nasdaq SmallCap Market on June 26, 2003. Each share of our common stock is accompanied by one share of our Series A junior participating preferred stock purchase rights that trades with the common stock. The value attributed to those rights, if any, is reflected in the market price of our common stock. Prior to the occurrence of certain events, none of which has occurred as of this date, the rights will not be exercisable or evidenced separately from the common stock.

(2) Represents shares issuable upon exercise of outstanding warrants. In accordance with Rule 416, there is also being registered hereunder such indeterminate number of additional shares of Common Stock as may become issuable upon exercise of the warrants to prevent dilution resulting from stock splits, stock dividends or similar transactions.

(3) Based, pursuant to Rule 457, on the exercise price of warrants.

(4) These warrants are exercisable at $3.05 per share, and the shares of Common Stock issuable upon exercise of these warrants are also being registered. Since a registration fee is being paid on the underlying shares of Common Stock, no separate registration fee is payable with respect to the warrants, pursuant to Rule 457.

(5) We previously paid a filing fee of $1,120.98 with the original filing of this Registration Statement.

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

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

SUBJECT TO COMPLETION, July 29, 2003.

PROSPECTUS

CYTRX CORPORATION

Common Stock

Warrants

All of the shares of our common stock and warrants to purchase shares of our common stock offered hereby are being sold by the securityholders listed in this prospectus. See Selling Securityholders. Each of the shares of our common stock is accompanied by one share of our Series A junior participating preferred stock purchase rights that trades with our common stock. Of the shares offered, 5,168,898 shares are owned by the selling securityholders as of the date of this prospectus and 2,763,955 shares are issuable upon the exercise of outstanding warrants to purchase our common stock held by certain of the selling securityholders, which includes warrants that are offered hereby to purchase 735,136 of those shares. The number of shares offered by the selling securityholders is subject to increase in certain events by reason of so-called antidilution provisions contained in the warrants held by them. The selling securityholders holding warrants must first exercise the warrants and acquire the underlying shares from us before they can resell those shares under this prospectus.

We will receive the exercise price of the warrants described in this prospectus to the extent they are exercised for cash, but we will not otherwise receive any proceeds in connection with the sale of the shares by the selling securityholders. See Use of Proceeds.

Our common stock is traded on the Nasdaq SmallCap Market under the symbol CYTR . On July 28, 2003, the last sale price for the common stock as reported on the Nasdaq SmallCap Market was $1.83. There is no public trading market for the warrants offered by this prospectus, and no public trading market is expected to develop for them.

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

We will bear the costs and expenses of registering the shares offered by the selling securityholders. The selling securityholders will bear any commissions and discounts attributable to their sales of the shares.

An investment in the common stock involves a high degree of risk. Before purchasing any shares, you should consider carefully the risks described under Risk Factors beginning on page 6.

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

The date of this prospectus is _____, 2003

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

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THE COMPANY

General

We are a Delaware corporation that was incorporated in 1985 and is engaged in the development and commercialization of pharmaceutical products. Subsequent to our acquisition of Global Genomics Capital in July 2002, we modified our corporate business strategy by discontinuing any further additional research and development efforts for any of our then existing technologies and by seeking strategic alliances, license partners or other collaborative arrangements with larger pharmaceutical companies to complete the development of these technologies. As part of our new corporate strategy, we have focused our efforts on acquiring new technologies and products, including products that are already being marketed or have been approved for marketing. We may acquire these technologies or products through a merger of one or more privately held companies possessing existing or potential products or technologies that we consider to be attractive, although we have not entered into any commitments to acquire or merge with any other company.

In April 2003, we acquired our first new technologies by entering into exclusive license agreements with the University of Massachusetts Medical School covering potential applications for the medical institution s proprietary gene silencing technology in the treatment of specified diseases, including those within the areas of obesity and type II diabetes, and covering the medical institution s proprietary technology with potential gene therapy applications within the area of cancer. There is growing scientific interest in various potential techniques to halt the activity or silence targeted genes that cause cells to produce undesirable proteins as a means for developing therapeutic products. In consideration of the licenses, we made certain cash payments to the University of Massachusetts Medical School totaling approximately $186,000 and issued it a total of 1,613,258 shares of our common stock.

In May 2003, we broadened our strategic alliance with the University of Massachusetts Medical School by acquiring an exclusive license from that institution covering a proprietary DNA-based HIV vaccine technology. In consideration of this license, we made certain cash payments to the University of Massachusetts Medical School totaling approximately $18,000 and issued it 215,101 shares of our common stock. Under our various license agreements, we will be required to make milestone payments to the University of Massachusetts Medical School based on the development of products utilizing the licensed technologies that could aggregate over time up to $13,610,000 if we successfully complete the development of six separate products, and we will be required to pay royalties based on future sales of any products that we commercialize.

As part of our strategic alliance with the University of Massachusetts Medical School, we also agreed to fund certain pre-clinical research at that medical school relating to the use of our technologies licensed from that institution for the development of therapeutic products within the fields of obesity and type II diabetes and certain

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other areas. Although we intend to internally fund the early stage development work for certain of these product applications, we may seek as part of our corporate business strategy to secure strategic alliances or license agreements with larger pharmaceutical companies to fund the early stage development work for other gene silencing product applications and for subsequent development of those potential products where we fund the early stage development work.

Our other products are 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. Sickle cell disease is an inherited disease caused by a genetic mutation of hemoglobin in the blood, and acute vaso-occlusive disorders are a blockage of blood flow caused by deformed or sickled red blood cells which can cause intense pain in sickle cell disease patients. We are currently seeking strategic partners to complete the development of FLOCOR, and TranzFect is currently being developed by our two licensees for this product, Merck & Co., Inc. and Vical Incorporated. We are seeking 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 B and C, flu, malaria and other viral diseases. (Adjuvants are agents added to a vaccine to increase its effectiveness.) We also have a portfolio of potential products and technologies in areas that include spinal cord injury, vaccine delivery and gene therapy. In addition, we own minority interests in two development stage genomics companies, which are described under Global Genomics.

Product Development

University of Massachusetts Medical School Programs

Through our strategic alliance and exclusive license agreements with the University of Massachusetts Medical School, we have acquired the rights to a portfolio of technologies, including a gene silencing technology with potential therapeutic applications in certain defined areas that include obesity and type II diabetes, a DNA-based HIV vaccine technology and a cancer therapeutic technology.

RNA interference (RNAi), commonly referred to as a form of gene silencing, has been shown to effectively silence a targeted gene within a living cell with great specificity and potency. 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 the technique of using a short piece of RNA to precisely target the messenger RNA from a specific gene. The end result is the silencing of that gene. RNAi is regarded as a significant advancement in gene silencing and recently was featured in the magazine Science as the Breakthrough of the Year in 2002. Delivery of RNAi can be used *in vitro* and *in vivo* to target specific mRNA (messenger RNA) to silence genes and to reduce the levels of the specific protein product coded for by that gene in the targeted cells. This will allow the use of RNAi either as a therapeutic product itself or as a drug discovery tool. We intend to develop the technology and then seek to demonstrate its efficacy in human clinical trials using RNAi to silence viral genes that cause disease or in small molecules developed from RNAi modeling to treat and prevent obesity and type II diabetes.

In mammals and human cells, RNAi can be triggered by delivering short double stranded RNA (dsRNA) molecules directly into the cell s cytoplasm (the region inside the cell membrane but outside the cell nucleus). Specific enzymes (proteins) called dicer enzymes in the cell cut the dsRNA to form small interfering RNA s (siRNAs). These siRNA are approximately 21 to 25 nucleotide long pieces of RNA. The siRNAs then interact with other cell enzymes called the RNA-Induced Silencing Complex, or RISC, which causes the unwinding of the bound siRNA. This unwound strand of the siRNA can bind with the complementary target messenger RNA (mRNA). The mRNA carries the coding (instructions) from the cell nucleus DNA. These instructions determine which proteins the cell is going to produce. When the siRNA binds with the mRNA, that message encounters interference, is not delivered, and the cell does not produce that specific protein. The siRNA can be designed to only interact with a single gene through its mRNA.

One reason for the potential of RNAi to be effective 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 RNA, where there were no enzymes present in the cells to facilitate the effectiveness of the antisense RNA molecule. In fact, one major problem with antisense has been the poor stability of the antisense product in the cell, caused by the cell recognizing it as a foreign material and trying to break it down. This is one of the reasons for the poor success rate to date for antisense RNA products.

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Another reason for the potential of RNAi to be effective is that it may be the first completely effective means of suppressing or eliminating a virus from cells. Once a virus is established in a cell, there are very few drugs that are effective in eliminating the virus (e.g., a cure for a viral disease). The RNAi process has the potential to eliminate viruses and, therefore, the potential to cure certain viral diseases. Development work on RNAi is still at an early stage, and we do not believe any clinical testing of medical applications using RNAi have yet been initiated.

Obesity and type II diabetes are becoming two of the most important health problems in the United States. According to the American Obesity Association, there are currently more than 55 million cases of obesity in the United States, and the American Diabetes Association reports that there are more than 16 million cases of type II diabetes in the United States alone. Scientists at the University of Massachusetts Medical School, as part of our license arrangement with that institution, are researching with funding that we have provided the specific genetic relationship of type II diabetes to obesity. The research is focused on using cultured adipocytes (fat cells) as a model system for studying insulin action on glucose transport, which is the movement of or uptake of glucose into the cell, and metabolic pathways, which are detailed outlines of how different components such as glucose are consumed within a cell. RNAi has the potential of being the only reliable method to selectively inhibit a gene or its protein expression in the cultured adipocytes. This research may lead to a better understanding of the insulin signaling pathway as well as metabolic pathways for glucose and fatty acids. With this understanding, the program will focus on drug discovery for type II diabetes (e.g., drugs that act as insulin sensitizers and compounds that alleviate obesity).

The HIV vaccine technology that we have licensed from the University of Massachusetts Medical School is based on a unique mixture of human HIV-1 primary isolates from several genetic subtypes of HIV. This 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. The University of Massachusetts Medical School has conducted animal studies of this vaccine, and that institution and another company providing an adjuvant for use with the vaccine have received a $15 million grant from the NIH, which will fund a Phase I clinical trial of a vaccine candidate using our licensed technology that is scheduled to begin in late 2003. According to the World Health Organization, in December 2002, more than 42 million people worldwide were living with HIV/AIDS. We also have licensed a cancer treatment technology from the University of Massachusetts Medical School that is based on a naked DNA approach in which the DNA material will be delivered by direct injection into the tumor or other localized administration.

Therapeutic Copolymer Programs

Our primary focus prior to our acquisition of Global Genomics was on CRL-5861 (purified poloxamer 188), which we also call FLOCOR for purposes of our potential sickle cell disease product. CRL-5861 may also provide benefits in cancer treatment when used in combination with radiation or cytotoxic drugs, which are drugs that can produce a toxic effect in cells.

Sickle cell disease is a devastating disorder originating from an inherited abnormality of hemoglobin, the oxygen-carrying molecule in red blood cells, which is typically seen in African-Americans and others of African descent.

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 (objective of the study), statistically significant and clinically important benefits associated with FLOCOR were observed in certain subgroups. In addition, among the entire patient population, treatment with FLOCOR resulted in a statistically significant increase in the percentage of patients achieving resolution of their crisis. The Phase III study also demonstrated that FLOCOR is well tolerated. Based on our conversations with the United States Food and Drug Administration (FDA), we believe it is likely that either two small additional pivotal trials or one large trial will be required for FLOCOR s approval, along with one to two additional safety studies.

Vaccine Enhancement and Gene Therapy

Gene therapy and/or 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.

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A large majority of our revenues over the past three years has been generated from license fees paid to us with respect to our TranzFect technology, representing 78%, 85% and 60% of our total revenues for 2002, 2001 and 2000, 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 targeted to four infectious diseases, one of which is HIV. To date, Merck has focused its efforts on the HIV application, which is still at an early stage of clinical development. In November 2000, Merck paid us a signature payment of $2 million and in February 2002, Merck paid us an additional $1 million milestone fee related to the commencement by Merck of the first FDA Phase I study for the first product incorporating TranzFect designed for the prevention and treatment of HIV. Merck will pay us additional milestone payments and royalties based on sales if certain development milestones are achieved and if Merck commercializes a product utilizing our TranzFect technology. All amounts paid to us 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) four infectious disease vaccine targets previously licensed by us to Merck, and (2) DNA vaccines or therapeutics based on prostate-specific membrane antigen (PSMA). 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). Vical has not yet commenced any clinical development work with our TranzFect technology. Under the Vical license, we received a non-refundable up-front payment of $3,750,000, and we have the potential to receive milestone and royalty payments in the future based on criteria described in the agreement. All amounts paid to us are non-refundable upon termination of the agreement and require no additional effort on our part.

Global Genomics

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

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

Global Genomics is a development stage company that has been engaged principally in investing in or acquiring companies that develop and commercialize healthcare products driven by genomics technologies. Global Genomics primary assets are a 40% equity interest in Blizzard Genomics, Inc. and a 5% equity interest in Psynomics, Inc.

Blizzard Genomics is developing instrumentation, software and consumable supplies for the growing genomics industry. Blizzard Genomics is the exclusive sublicensee of a technology that it believes allows for cheaper, faster and more portable analysis of DNA, through the use of its

own readers and DNA chips, as compared to other currently available technology. Subject to having sufficient financial resources, Blizzard Genomics has plans to commercially launch its first product, a chip reader, during late 2003 or early 2004. Since Blizzard Genomics current products are primarily for use in research laboratories, they will not need to be approved by the FDA before they can be marketed.

Psynomics is an early stage psychiatric genomics company. Psynomics is currently operating out of the University of California, San Diego as a virtual company with no full-time or salaried employees, facilities or other corporate or research infrastructure and has had an ongoing research collaboration with its founders at that

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university. Psynomics goal is to develop technology for the diagnosis and treatment of neuropsychiatric diseases, but it has not yet commenced any work in this area.

The shares of our common stock that we issued in the merger with Global Genomics or that we will issue upon exercise of warrants issued by Global Genomics that we assumed in the merger were not registered under the Securities Act. However, pursuant to a registration rights agreement that we signed with the former shareholders of Global Genomics, we have filed a registration statement to register under the Securities Act the resale of these shares, together with certain other shares of our common stock that we issued or that are issuable upon the exercise of warrants that we have issued to third parties.

Recent Developments

In May 2003, we completed a $5,440,000 private equity financing to a group of institutional investors in which we issued 2,940,539 shares of our common stock and warrants to purchase an additional 735,136 shares of our common stock at an exercise price of $3.05 per share. The proceeds of this financing will be available for our general working capital, including for funding payments that we will be required to make in connection with our strategic alliance with the University of Massachusetts Medical School. This prospectus is part of the registration statement that we filed as a result of our agreement to register for resale under the Securities Act the shares of common stock, the warrants and the shares of common stock issuable upon exercise of the warrants sold in this financing and the shares that we issued to the University of Massachusetts Medical School in connection with our strategic alliance with that institution. This prospectus also covers the resale of certain other shares of our common stock that we issued or that are issuable upon the exercise of warrants that we have issued to third parties.

RISK FACTORS

You should carefully consider the following risks before deciding to purchase shares of our common stock. If any of the following risks actually occur, the trading price of our common stock could decline, and you could lose all or part of your investment. You should also refer to the other information in this prospectus and the information incorporated into this registration statement by reference, including our financial statements and the related notes.

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

We have incurred significant losses over the past five years, including net losses of approximately $914,000 for the three months ended March 31, 2003 (on an unaudited basis) and $6,176,000, $931,000 and $348,000 for 2002, 2001, and 2000, respectively, and we had an accumulated deficit of approximately $72,871,000 as of March 31, 2003 (on an unaudited basis). 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, as we generate significant recurring revenues. Unless we are able to acquire products from third parties that are already being marketed and that can be profitably marketed by us, it will take an extended period of time for us to generate recurring revenues. We anticipate that it will take at least several years before the development of any of our licensed or other current potential products is completed, FDA marketing approvals are obtained and commercial sales of any of these products can begin.

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

Although we generated $3,751,000 in revenues from milestone payments from our licensees during 2001 and $1,001,000 from these sources during 2002, we do not have any significant sources of recurring operating revenues. We will not have significant recurring operating revenues until at least one of the following occurs:

- one or more of our currently licensed products is commercialized by our licensees that generates royalty income for us
- we are able to enter into license or other arrangements with third parties who are then able to complete the development and commercialize one or more of our other products that are currently under development
- we are able to acquire products from third parties that are already being marketed or are approved for marketing

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We are likely to incur negative cash from operations until such time, if ever, as we can generate significant recurring revenues. Should we be unable to generate these recurring revenues after the next 24 months, it is likely that we will become dependent on obtaining financing from third parties to meet our obligations to the University of Massachusetts Medical School and maintain our operations. We have no commitments from third parties to provide us with any debt or equity financing. Accordingly, financing may be unavailable to us or only available on terms that substantially dilute our existing shareholders. A lack of needed financing could force us to reduce the scope of or terminate our operations or to seek a merger with or be acquired by another company. There can be no assurance that we would be able to identify an appropriate company to merge with or be acquired by or that we could consummate such a transaction on terms that would be attractive to our shareholders 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 78%, 85% and 60% of our total revenues for 2002, 2001 and 2000, respectively. We have already licensed most of the potential applications for this technology, and there can be no assurance that we will be able to generate additional license fee revenues from any new licensees for this technology. Our current licensees for TranzFect (Merck and Vical) may be required to make further milestone payments to us under their licenses based on their future development of products using TranzFect. However, Merck is at an early stage of clinical trials of a product utilizing TranzFect, and Vical has not yet commenced any clinical trials of a product utilizing TranzFect. 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 to Find and Rely Upon Third Parties for the Development of Our Products and to Provide Us With Products

We have modified our prior business strategy of internally developing FLOCOR and our other potential products not yet licensed to third parties. We will now seek to enter into strategic alliances, license agreements or other collaborative arrangements with larger pharmaceutical companies that will provide for those companies to be responsible for the development and marketing of our products, although we intend to internally fund the early stage development work for certain product applications based on the gene silencing and other technologies that we have licensed from the University of Massachusetts Medical School. There can be no assurance that our products will have sufficient potential commercial value to enable us to secure these arrangements with suitable companies on attractive terms or at all. If we enter into these arrangements, we will be dependent upon the timeliness and effectiveness of the development and marketing efforts of our contractual partners. If these companies do not allocate sufficient personnel and resources to these efforts or encounter difficulties in complying with applicable FDA 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. If we are unable to enter into these arrangements for a particular product, we may be required to either sell the product to a third party or abandon it unless we are able to raise sufficient capital to fund the substantial expenditures necessary for development and marketing of the product.

We will also seek to acquire products from third parties that already are being marketed or have previously been marketed. We have not yet identified any of these products. It may be difficult for us to acquire these types of products with our limited financial resources, and we may incur substantial shareholder dilution if we acquire these products with our securities. 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 privately held companies that own such products. Although we anticipate that we would be the surviving company in any such merger, the owners of the private company could be issued a substantial or even controlling amount of stock in our company.

Our Limited Financial Resources May Adversely Impact Our Ability to Execute Certain Strategic Initiatives

On March 31, 2003 we had approximately $1,281,000 in cash and cash equivalents and approximately $1,157,000 in working capital. (Our cash and working capital position have significantly improved since March 31, 2003, primarily as the result of our completing a $5,440,000 private equity financing in May 2003.) Our recently modified product development strategy calls for seeking strategic alliances, licensing agreements or other collaborative arrangements with larger pharmaceutical companies to complete the development of FLOCOR and our other potential products, and we will not continue any further FLOCOR development work on our own in the

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meantime. Although we are not doing any further development work on TranzFect, our two licensees for this technology (Merck & Co. and Vical Incorporated) are continuing to do development work on product applications for this technology that could entitle us to future milestone payments should they continue with this work and it successfully meets the defined milestones, as well as future royalty payments should either of these licensees commercialize products based on our technology. However, there can be no assurance that our licensees will continue to develop or ever commercialize any products that are based on our TranzFect technology.

Our strategic alliance with the University of Massachusetts Medical School may require us to make significant expenditures to fund research at that medical institution relating to developing therapeutic products based on that institution s proprietary technology that has been licensed to us. We estimate that the aggregate amount of these sponsored research expenditures under certain circumstances could range from approximately $1,600,000 to $1,800,000 annually over the next three years. Our license agreements with the University of Massachusetts Medical School also provide in certain cases for milestone payments based on the progress made by us in the clinical development of products utilizing the technologies licensed from the University of Massachusetts Medical School and marketing of these products. These milestone payments could aggregate over time up to $13,610,000 if we successfully complete the development of six separate products.

Our potentially required expenditures under our agreements with the University of Massachusetts Medical School could substantially exceed our current financial resources and require us to raise additional capital or secure a licensee or strategic partner to fulfill our obligations to the University of Massachusetts Medical School and to develop any products based on the technology that we have licensed from that medical institution. If we are unable to meet our various financial obligations under these license agreements, which included a requirement that we raise at least $10,000,000 of additional capital within 18 months after the signing of these agreements, we could lose all of our rights under these agreements.

We also will seek to acquire products from third parties that already are being or have previously been marketed or are approved for marketing. Although we believe this strategy will enhance our ability to achieve profitability, our lack of substantial available funds may make it difficult for us to acquire new products or to adopt other strategic initiatives in the future, such as acquiring or developing a marketing organization for our products or resuming internal development work on our products.

Our Recent Acquisition of Global Genomics May Place Additional Financial and Operational Burdens on Us

In July 2002, we acquired Global Genomics through a merger. Global Genomics is a development stage company that, to date, has not generated any operating revenue, does not expect to generate any revenues in the foreseeable future and has operated at a loss since its organization in May 2000. Global Genomics had a cumulative loss from inception through March 31, 2003 (on an unaudited basis) of approximately $2,190,000, a loss of approximately $71,000 for the three months ended March 31, 2003 (on an unaudited basis), and a loss of approximately $303,000 and $1,563,000 for 2002 and 2001, respectively. We have moved our headquarters in connection with the merger to Los Angeles, California while we continue to incur a substantial lease expense ($14,000 per month, less offsetting sublease income of currently $3,000 per month) for our prior headquarters in Norcross, Georgia. We may be unable to substantially mitigate the future rental expense for our prior headquarters by subleasing this space.

Although a majority of the members of our board of directors were directors prior to our merger with Global Genomics, all of our then current operating officers were terminated as a part of the merger. This change in personnel may place additional administrative burdens on our management in conducting our operations.

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

Each of our products is in the development stage 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 currently anticipate due to numerous factors such as:

- difficulty in securing centers to conduct trials
- difficulty in enrolling patients in conformity with required protocols or projected timelines
- unexpected adverse reactions by patients in trials
- difficulty in obtaining clinical supplies of the product
- changes in the FDA s requirements for our testing during the course of that testing

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

The gene silencing and other technologies that we have acquired from the University of Massachusetts Medical School have not yet been clinically tested by us, nor are we aware of any clinical trials having been conducted by third parties involving similar gene silencing technologies. Our TranzFect technology is currently in Phase I clinical trials that are being conducted by our licensee, Merck & Co., as a component of a vaccine to prevent AIDS. Since TranzFect is to be used as a component in vaccines, we do not need to seek FDA approval, but the vaccine manufacturer will need to seek FDA approval for the final vaccine formulation containing TranzFect.

We Were Only Able to Establish the Effectiveness of FLOCOR in a Subset of Patients in a Recent Clinical Trial and May Be Unable to Establish a Viable Medical Indication for FLOCOR or Find a Partner to Fund the Necessary Research for FLOCOR

In December 1999, we reported results from our Phase III clinical trial of FLOCOR for treatment of sickle cell disease patients experiencing an acute vaso-occlusive crisis. Overall, the study was not able to achieve its primary objective, which was to show a statistically significant decrease in the length of vaso-occlusive crisis for the study population as a whole. However, for patients 15 years of age or younger, the number of patients achieving 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. We believe that there were certain design flaws in the protocol for the previous Phase III clinical trial relating primarily to the assumed period for resolution of a vaso-occlusive crisis in patients not treated with FLOCOR that may have impacted the results of that clinical trial and that would need to be addressed in properly designing any future trial.

To generate sufficient data to seek FDA approval for FLOCOR will require additional clinical studies, which will entail substantial time and expense. We currently estimate the cost of these clinical trials to be in the range of $10,000,000 $12,000,000, although the actual costs could vary substantially, depending on the nature and number of trials that the FDA ultimately would require. We do not intend to conduct or fund these tests ourselves but will seek a strategic alliance partner or licensee for this purpose. The failure of our prior Phase III trial to generate sufficient data could make it more difficult for us to secure a strategic alliance partner or licensee for this product. In June 2002, the National Heart, Lung and Blood Institute of the National Institutes of Health turned down a grant application by Johns Hopkins University School of Medicine to provide financial support for a potential new Phase III trial for FLOCOR. Since this grant application was submitted at the NIH s suggestion, we believed that there was a reasonable possibility of obtaining governmental funding for the cost of a new FLOCOR trial. However, based on the NIH s rejection of the Johns Hopkins application, we may encounter difficulty in obtaining future governmental financial support for FLOCOR development work should we or any strategic partner or licensee seek such support in the future.

If Blizzard Genomics Fails to Successfully Commercialize Its Products, the Value of Our Assets Will Be Adversely Impacted

Blizzard Genomics, Inc., which is Global Genomics principal portfolio company, has not yet commercialized any of its products. Although Blizzard Genomics plans to introduce its first product, the I-Scan Imager, a low cost DNA chip reader, in late 2003 or early 2004, it may experience delays in completing the development of or commercially launching this product. Blizzard Genomics products will be used in research laboratories and will not require FDA approval prior to their being marketed. These products are likely to face intense market competition from existing products or technologies and products or technologies that are developed in the future. Blizzard Genomics is the licensee of several U.S. patents, and is seeking additional patent protection for its products and technologies. There can be no assurance, however, that the company will be able to secure sufficient patent coverage for its products and technologies. The failure of Blizzard Genomics to successfully commercialize its products would require us to write down or write off the substantial carrying value of Global Genomics investment in that company as part of our assets, which would have a materially adverse effect on our stockholders equity.

Blizzard Genomics May Be Unable to Raise Sufficient Funding to Commercialize Its Products, Which Would Adversely Impact the Value of Our Assets

Blizzard Genomics has no working capital and is currently seeking to raise up to $2,000,000 in capital to fund the commercial launch of the I-Scan Imager and for its working capital needs. Blizzard Genomics has encountered difficulty to date in obtaining this capital. Failure to raise at least a portion of this capital could delay

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Blizzard Genomics commercialization of its products and might force it to suspend its operations. Should Blizzard Genomics raise at least $750,000 in capital, it believes that it would have sufficient funding to begin commercial marketing of the I-Scan Imager but would require additional capital to complete development of any other products and might need additional capital to support its operations. Any significant delay in the commercialization of Blizzard Genomics products or the cessation of its operations would adversely affect the carrying value of Global Genomics investment in that company as part of our assets, which would have a materially adverse effect on our stockholders equity. Although we may consider making a further investment in Blizzard Genomics, we have not discussed the terms of any such investment with Blizzard Genomics and have no obligation to make any new investment in that company.

We Are Dependent Upon a Limited Operational Management Team and Need to Recruit a Chief Financial Officer and Perhaps Other Personnel to Effectively Operate

Our current management team is limited to Steven A. Kriegsman, our Chief Executive Officer and interim Chief Financial Officer, and Kathryn H. Hernandez, our Corporate Secretary. We are, therefore, very dependent on the availability and quality of the efforts of Mr. Kriegsman in managing our company. We will need to recruit a permanent Chief Financial Officer and may need to recruit other personnel in order to effectively operate the company and carry out our business plan.

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 earlier than we or our strategic partners or licensees
- Obtain approvals for such products from the FDA or other regulatory agencies more rapidly than we or our strategic partners or licensees do
- Obtain patents that block or otherwise inhibit the development and commercialization of our product candidates
- Develop treatments or cures that are safer or more effective than those we propose for 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 make the continued development of our product candidates uneconomical

Withstand price competition more successfully than our strategic partners or licensees can

More effectively negotiate third-party strategic alliances or licensing arrangements

Take advantage of product acquisition or other opportunities more readily than we can

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 (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, we would compete against companies that are developing or marketing other products to treat sickle cell disease, such as Droxia (hydroxyurea) marketed by Bristol-Myers

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Squibb Co. and Decitabine, which is being developed by SuperGen, Inc. Our TranzFect technology will compete against a number of companies that have developed adjuvant products, such as the adjuvant QS-21 marketed by Aquila Biopharmaceuticals, Inc. and adjuvants marketed by Corixa. Blizzard Genomics products will compete with a number of currently marketed products, including those offered by Axon Instruments, Affymetrix, Applied Precision, Perkin Elmer and Agilent Technologies. A number of medical institutions and pharmaceutical companies are seeking to develop products based on gene silencing technologies. Companies working in this area include Sirna Therapeutics, Inc., Ribopharma A.G., Alnylam, Inc., Benitec, Nucleonics, Inc. and a number of the multinational pharmaceutical companies. Companies developing HIV vaccines that could compete with our product include Merck, VaxGen, AlphaVax and Immunitor Corporation.

The Manufacturing Requirements for FLOCOR May Make It More Difficult for Us to License FLOCOR or for Our Licensee to Develop FLOCOR

The manufacture of CRL-5861 requires the following:

- a supply of the raw drug substance
- a supply of the purified drug which is refined from the raw drug substance
- formulation and sterile filling of the purified drug substance into the finished drug product

A number of suppliers and manufacturers can provide the raw drug substance and the finished drug product. Prior to the change in our business strategy to now seek a strategic partner or licensee for FLOCOR (who we anticipate would be responsible for the manufacture of FLOCOR), we entered into an agreement with Organichem Corp. to provide us with commercial supplies of the purified drug substance. However, this agreement will expire before the end of 2003, which will be well before any potential strategic partner or licensee that we might secure will need commercial supplies of this substance. There can be no assurance that any strategic partner or licensee that we secure will either have the specific equipment expertise to purify the FLOCOR drug substance or will be able to enter into an agreement with Organichem or another supplier on acceptable terms. An inability to obtain purified drug substance in sufficient amounts and at acceptable prices could have a material adverse effect on our ability to secure a strategic partner or licensee or on the ability of that partner or licensee to commercialize FLOCOR.

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

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 our FLOCOR and TranzFect technologies, there can be no assurance that this coverage will be broad enough to prevent third parties from developing or commercializing similar or identical technologies, that the validity of our patents will be upheld if challenged by third parties or that our technologies will not be deemed to infringe the intellectual property rights of third parties. We have a non-exclusive license to a patent owned by the University of Massachusetts Medical School and another institution that covers the general field of gene silencing. The specific medical applications of the gene silencing technology and the other technologies that we have licensed from the University of Massachusetts Medical School are covered by a number of pending patent applications. However, other researchers have been active in the field of gene silencing, and these 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. Any litigation brought by us to protect our intellectual property rights or by third parties asserting intellectual property rights against us could be costly and have a material adverse effect on our operating results or financial condition and make it more difficult for us to enter into strategic alliances with third parties to develop our products or discourage our existing licensees from continuing their development work on our potential products. If our patent coverage is insufficient to prevent third parties from developing or

commercializing similar or identical technologies, the value of our assets is likely to be materially and adversely affected.

We 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

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caused unintended adverse effects. We currently do not carry product liability insurance covering the use of our products in human clinical trials or the commercial marketing of these products but 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 the insurance coverage of our licensees or their other financial resources are inadequate to cover a successful claim, such successful claim may exceed our financial resources and 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.

It Will Be Difficult For Us To Manage Our Operations If We Are Regulated As An Investment Company In The Future

The Investment Company Act of 1940 regulates certain companies that own investment securities with a value greater than 40% of the total assets of that company. In the Global Genomics merger, we acquired a 40% equity interest in Blizzard Genomics, Inc., which investment represented approximately 76% of our total assets as of March 31, 2003. Accordingly, because our investment in Blizzard Genomics represents such a large percentage of our total assets, we would be subject to the Investment Company Act if an exemption were not available. The SEC s regulations, however, exempt certain companies from the Investment Company Act if they, among other things, have a controlling interest in the subsidiary company. While we believe this exemption is currently available to us, if our ownership interest in Blizzard Genomics significantly decreases or we otherwise no longer remain the largest shareholder of Blizzard Genomics, the value of our investment in Blizzard Genomics could cause us to become subject to the provisions of the Investment Company Act. Should we become subject to the Investment Company Act, we would essentially have to operate as a mutual fund and would be subject to all of the substantive regulations imposed on such companies, including the restrictions on the securities we can issue, the rules specifying the composition and structure of our management, the additional reporting requirements, and other limitations on our ability to conduct our operations in the manner currently conducted. Our Board of Directors has determined that, should we become subject to these provisions, we will either (i) seek an order from the SEC exempting us from these provisions, or (ii) attempt to restructure our business in a manner that would relieve us from these provisions. The regulatory requirements for investment companies are extremely restrictive and would materially and adversely affect our ability to manage and operate our business and could materially and adversely affect our financial condition. Although it is our intention to remain an operating company that is not subject to the Investment Company Act, no assurance can be given that we will not become subject to the provisions of that act.

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

We have a shareholder rights plan and provisions in our bylaws that may discourage or prevent a person or group from acquiring us without our board of directors approval. The intent of the shareholder rights plan and our bylaw provisions is to protect our shareholders 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 shareholders from seeking to change our existing management in order to change the strategic direction or operational performance of our company.

Our bylaws provide that directors may only be removed for cause by the affirmative vote of the holders of at least a majority of the outstanding shares of our capital stock then entitled to vote at an election of directors. This provision prevents stockholders from removing any incumbent director without cause. Our bylaws also provide that a stockholder must give us at least 120 days notice of a proposal or director nomination that

such stockholder desires to present at any annual meeting or special meeting of stockholders. Such provision prevents a stockholder from making a proposal or director nomination at a stockholder meeting without us having advance notice of that proposal or director nomination. This could make a change in control more difficult by providing our directors with more time to prepare an opposition to a proposed change in control. By making it more difficult to remove or install new directors, the foregoing bylaw provisions may also make our existing management less responsive to the views

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of our shareholders 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, in Our Recent Private Financing and to the University of Massachusetts Medical School May Adversely Affect the Trading Price of Our Common Stock