

CYTRX CORP
Form 424B3
May 21, 2007

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As filed pursuant to Rule 424(b)(3)
Under the Securities Act of 1933
Registration No. 333-142591

**PROSPECTUS
CYTRX CORPORATION
8,765,000 Shares
Common Stock**

This prospectus relates to shares of our common stock being offered for sale by the selling stockholders listed in this prospectus under Selling Stockholders. Each of the shares is accompanied by one Series A Junior Participating Preferred Stock Purchase Right that trades with our common stock.

We will not receive any proceeds from the sale of the shares by the selling stockholders. We will bear the costs and expenses of this offering, except that the selling stockholders will bear any commissions and discounts attributable to their sales of the shares.

Our common stock is traded on the Nasdaq Capital Market under the symbol CYTR. On May 18, 2007, the last sale price of our common stock as reported on the Nasdaq Capital Market was \$4.03.

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

An investment in our shares involves a high degree of risk. Before purchasing any shares, you should consider carefully the risks described under Risk Factors beginning on page 5.

NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED THESE SECURITIES OR DETERMINED THAT THIS PROSPECTUS IS COMPLETE OR ACCURATE. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

The date of this prospectus is May 21, 2007

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed on behalf of the selling stockholders with the Securities and Exchange Commission, or the SEC, to permit the selling stockholders to sell the shares described in this prospectus in one or more transactions. The selling stockholders and the plan of distribution of the shares being offered by them are described in this prospectus under the headings "Selling Stockholders" and "Plan of Distribution."

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

In this prospectus, we sometimes refer to CytRx Corporation as "CytRx" and to its majority-owned subsidiary, RXi Pharmaceuticals Corporation, as "RXi." References in this prospectus to the company, we, us or our refer to CytRx, RXi, unless the context suggests otherwise.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the informational requirements of the Securities Exchange Act of 1934, or Exchange Act, and are required to file annual, quarterly and other reports, proxy statements and other information with the SEC. You may inspect and copy these reports, proxy statements and other information at the public reference facilities maintained by the SEC in Washington, D.C. (100 F Street NE, Room 1580, Washington, D.C. 20549). Copies of such materials can be obtained from the SEC's public reference section at prescribed rates. You may obtain information on the operation of the public reference rooms by calling the SEC at (800) SEC-0330 or on the SEC website located at <http://www.sec.gov>.

Our common stock is traded on the Nasdaq Capital Market under the symbol "CYTR." Reports, proxy and information statements and other information concerning us also may be inspected at the offices of the National Association of Securities Dealers, Inc. located at 1735 K Street, N.W., Washington, D.C. 20006.

Information about us is also available at our website at <http://www.cytrx.com>. However, the information on our website is not a part of this prospectus.

INCORPORATION OF INFORMATION FILED WITH THE SEC

The SEC allows us to incorporate in this prospectus by reference information contained in documents that we file with the SEC, which means that we can disclose important information to you by referring you to those other documents. The information incorporated by reference is an important part of this prospectus, and documents that we file with the SEC after the date of this prospectus will automatically update and, where applicable, modify or supersede any information set forth or incorporated by reference in this prospectus.

We incorporate by reference in this prospectus the documents listed below:

Our Annual Report on Form 10-K for the year ended December 31, 2006;

Our Current Reports on Form 8-K filed on January 9, 2007, January 6, 2007, February 5, 2007, February 6, 2007, February 21, 2007, February 28, 2007, April 2, 2007, April 3, 2007, April 18, 2007, April 20, 2007, April 24, 2007 and May 1, 2007.

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The description of our common stock as described in our Registration Statement on Form 8-A filed under the Exchange Act on March 17, 1987 (File No. 0-15327), and any amendment or report filed for the purpose of updating any such description.

The description of our Series A Junior Participating Preferred Stock Purchase Rights as described in our Registration Statement on Form 8-A filed under the Exchange Act on April 17, 1997 (File No. 000-15327), and any amendment or report filed for the purpose of updating any such descriptions.

Any document that we file with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus and before the termination of this offering (other than any portion of such documents that are not deemed filed under the Exchange Act in accordance with the Exchange Act and applicable SEC rules). Information in these subsequent SEC filings will be deemed to be incorporated by reference as of the date we make the filing.

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

NOTE ON FORWARD-LOOKING STATEMENTS

Some of the statements under Risk Factors, About CytRx, About RXi and elsewhere in this prospectus may include forward-looking statements that reflect our current views with respect to our research and development activities, business strategy, business plan, financial performance and other future events. These statements include forward-looking statements both with respect to us, specifically, and the biotechnology sector, in general. We make these statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Statements that include the words expect, intend, plan, believe, project, estimate, may, should, anticipate, similar statements of a future or forward-looking nature identify forward-looking statements for purposes of the federal securities laws or otherwise.

All forward-looking statements involve inherent risks and uncertainties, and there are or will be important factors that could cause actual results to differ materially from those indicated in these statements. We believe that these factors include, but are not limited to, those factors set forth in this prospectus under the caption Risk Factors and in our most recent Annual Report on Form 10-K under the captions Business, Legal Proceedings, Management's Discussion and Analysis of Financial Condition and Results of Operations, Quantitative and Qualitative Disclosures About Market Risk and Controls and Procedures, all of which you should review carefully. Please consider our forward-looking statements in light of those risks as you read this prospectus. We undertake no obligation to publicly update or review any forward-looking statement, whether as a result of new information, future developments or otherwise.

If one or more of these or other risks or uncertainties materializes, or if our underlying assumptions prove to be incorrect, actual results may vary materially from what we anticipate. All subsequent written and oral forward-looking statements attributable to us or individuals acting on our behalf are expressly qualified in their entirety by this note. Before purchasing any shares, you should consider carefully all of the factors set forth or referred to in this prospectus that could cause actual results to differ.

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SUMMARY

The following is only a summary of this prospectus and does not contain all of the information that you should consider before deciding whether to purchase any shares. You should read carefully this entire prospectus, including the Risk Factors section, as well as the information set forth or referred to in this prospectus under the captions Where You Can Find More Information and Incorporation of Information Filed With The SEC.

CytRx Corporation

CytRx is a biopharmaceutical research and development company engaged in developing human therapeutic products based primarily upon our small molecule molecular chaperone co-induction technology. We recently completed a Phase IIa clinical trial of our lead small molecule product candidate, arimoclomol, for the treatment of amyotrophic lateral sclerosis, which is commonly known as ALS or Lou Gehrig's disease. Arimoclomol has received Orphan Drug and Fast Track designation from the U.S. Food and Drug Administration, or FDA, and orphan medicinal product status from the European Commission for the treatment of ALS. We plan to initiate a Phase IIb trial of arimoclomol for this indication during the second half of 2007, subject to FDA clearance. Recent preclinical animal studies indicated that arimoclomol accelerated the recovery of sensory and motor functions following a stroke, even when administered up to 48 hours after the stroke. Based upon these positive indications, we are considering a possible Phase II clinical trial of arimoclomol in stroke patients. We also are pursuing clinical development of our other small molecule product candidates, as well as 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 with funding from the National Institutes of Health. See the section About CytRx in this prospectus for more information regarding our product candidates and research and development activities. We also are engaged through RXi Pharmaceuticals Corporation, or RXi, our majority-owned subsidiary, in developing therapeutic products based upon ribonucleic acid interference, or RNAi.

Our corporate offices are located at 11726 San Vicente Boulevard, Suite 650, Los Angeles, California 90049, and our telephone number is (310) 826-5648. We maintain a laboratory facility located at One Innovation Drive, Worcester, Massachusetts 01605, which also houses the corporate offices and research facilities of RXi.

RXi Pharmaceuticals Corporation

Our board of directors periodically reviews and assesses strategic alternatives for our company, and determined that the best strategy for realizing the potential value of our RNAi technologies was to create a subsidiary focused on RNAi therapeutics. RXi, our RNAi therapeutics subsidiary, was formed by CytRx and four leading RNAi researchers, including Craig C. Mello, Ph.D., who was awarded the 2006 Nobel Prize in Medicine for his co-discovery of RNAi. In January 2007, we transferred to RXi substantially all of our RNAi-related technologies and assets in exchange for equity in RXi. The transferred technologies and assets consisted primarily of our licenses from UMMS and the Carnegie Institution of Washington relating to fundamental RNAi technologies, as well as research and other equipment situated at our Worcester, Massachusetts, laboratory. RXi is focused solely on developing and commercializing therapeutic products based upon RNAi technologies for the treatment of human diseases, with an initial focus on neurodegenerative diseases, cancer, type 2 diabetes and obesity. See the section About RXi in this prospectus for a description of the technologies, research and development activities and current business plan of RXi.

Recent Development

We have agreed with UMMS and the other current stockholders of RXi that we will reduce our ownership interest in RXi's capital stock to less than a majority as soon as reasonably practicable. In order to do so, we intend to make a dividend or distribution of a portion of our RXi shares to our stockholders. Any future dividend or other distribution to our stockholders of RXi shares would be subject to the approval of our

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board of directors and to compliance with SEC rules and the requirements of the Delaware General Corporation Law, and there is no assurance as to the timing or amount of such dividend or distribution. Any such dividend or distribution would likely be taxable to our stockholders.

The Offering

On April 19, 2007, we sold 8,615,000 shares of our common stock to the selling stockholders pursuant to purchase agreements under which we agreed, within 15 days of that date, to file with the SEC a registration statement with respect to the resale of the shares by the selling stockholders. We also agreed in the purchase agreements to use our reasonable efforts to cause the registration statement to be declared effective under the Securities Act within a specified period of time, and in any event not later than 90 days after the closing date. We have complied with these obligations. We further agreed to keep the registration statement effective until the earliest of (i) two years after the effective date of the registration statement, (ii) such time as all of the shares have been sold pursuant to the registration statement, and (iii) such time as the shares become eligible for resale by non-affiliates pursuant to Rule 144(k) under the Securities Act or any other rule of similar effect. See the section **Plan of Distribution** for more information regarding this offering. The shares offered for sale under this prospectus also include 150,000 shares that we issued in December 2006 as payment under a license agreement with UMMS.

Issuer	CytRx Corporation
Selling Stockholders	The selling stockholders who are offering the shares for sale under this prospectus are named in the section Selling Stockholders in this prospectus or in a supplement to this prospectus.
Shares Offered	8,765,000 shares of our common stock, \$0.001 par value per share.
Shares Outstanding	87,341,129 shares as of April 30, 2007, excluding 22,358,822 shares subject to outstanding stock options and warrants.
Use of Proceeds	The selling stockholders will receive all proceeds from the sale of shares under this prospectus. We will not receive any proceeds from the sale of the shares by the selling stockholders.
Trading	Our common stock is traded on the Nasdaq Capital Market under its symbol CYTR.

Risk Factors

An investment in our shares involves a high degree of risk, including those relating to our ownership of RXi. You should consider carefully the risks described in the **Risk Factors** section of this prospectus before purchasing any shares.

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RISK FACTORS

An investment in our shares involves a high degree of risk. Before purchasing any shares, you should consider carefully the risks set forth below, as well as other information set forth or incorporated by reference in this prospectus. Risks and uncertainties not presently known to us, or that we currently deem to be immaterial, also may affect our business and operations.

Risks Associated With Our Business

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

We have operated at a loss due to our lack of significant recurring revenue combined with our substantial expenditures for research and development of our products and general and administrative expenses. We incurred net losses of \$16.8 million, \$15.1 million and \$16.4 million for the years ended December 31, 2006, 2005 and 2004, respectively, and had an accumulated deficit of approximately \$139.6 million as of December 31, 2006. We are likely to continue to incur losses unless and until, if ever, we are able to commercialize one or more of our products and generate significant recurring revenue.

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

Our revenue was \$2.1 million, \$184,000 and \$428,000 during the years ended December 31, 2006, 2005 and 2004, respectively. Of the \$2.1 million of revenue in 2006, \$1.8 million related to our sale to the ALS Charitable Remainder Trust of a one-percent royalty interest in worldwide sales of arimoclomol. We will not have other significant recurring revenue until at least one of the following occurs:

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

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

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

We have relied primarily upon proceeds from sales of our equity securities, including proceeds received upon the exercise of options and warrants, to generate funds needed to finance our business and operations. At December 31, 2006, we had cash and cash equivalents of \$30.4 million, and as of April 30, 2007, we had received approximately \$13.0 million in connection with the exercise of warrants and options since December 31, 2006. In addition, on April 19, 2007, we received \$19.2 million from the sale of shares to the selling security holders, net of offering expenses of approximately \$2.8 million and the \$15.0 million of net proceeds that we provided to RXi on April 30, 2007 to satisfy the initial funding requirements under its agreements with UMMS. We believe that our remaining current financial resources will be adequate to support our currently planned level of operations into the second half of 2009. This estimate is based in part on projected expenditures for 2007 of \$4.5 million for our Phase IIB trial of arimoclomol for ALS and related studies, \$4.4 million for our other ongoing and planned preclinical programs, including a possible Phase II clinical trial of arimoclomol in stroke patients, and \$8.8 million for general and administrative expenses. We estimate that RXi separately will expend approximately \$6.2 million on development activities for 2007 (including approximately \$400,000 in cash payments under agreements with UMMS, \$3.2 million in other research and development expenses and \$2.6 million in general and administrative expenses). We anticipate it will take a minimum of three years, and possibly longer, for us to generate recurring revenue, and we will be dependent on obtaining future financing until such time, if ever, as we can generate significant recurring revenue. We have no commitments from third

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parties to provide us with any financing, and may not be able to obtain financing on favorable terms, or at all. A lack of needed financing might force us to reduce the scope of our long-term business plans.

We Will Be Reliant Upon Third Parties for the Development and Eventual Marketing of Our Products

Our business plan is to enter into strategic alliances, license agreements or other collaborative arrangements with other pharmaceutical companies under which those companies will be responsible for the commercial development and eventual marketing of our products. Although we plan to continue the development of arimoclomol for the treatment of ALS and may market it ourselves if it is approved by the FDA, the completion of the development of our current product candidates, as well as the manufacture and marketing of these products, will likely require us to enter into strategic arrangements with other pharmaceutical or biotechnology companies.

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

To the extent we enter into collaborative arrangements, we will be dependent upon the timeliness and effectiveness of the development and marketing efforts of our contractual partners. If these companies do not allocate sufficient personnel and resources to these efforts or encounter difficulties in complying with applicable FDA and other regulatory requirements, the timing of receipt or amount of revenue from these arrangements may be materially and adversely affected. By entering into these arrangements rather than completing the development and then marketing these products on our own, we may suffer a reduction in the ultimate overall profitability for us of these products. In addition, if we are unable to enter into these arrangements for a particular product, we may be required to either sell our rights in the product to a third party or abandon it unless we are able to raise sufficient capital to fund the substantial expenditures necessary for development and marketing of the product.

We Will Incur Substantial Expenses and May Be Required to Pay Substantial Milestone Payments Relating to Our Product Development Efforts

We estimate that our clinical program for arimoclomol for the treatment of ALS, including the completion of the planned Phase IIb clinical trial and related studies, will require us to incur approximately \$23.0 million (including amounts payable under the Master Agreement for Clinical Trials Management Services we have entered into with Pharmaceutical Research Associates) over the next two to three years, assuming we receive FDA clearance for this trial. In addition, our agreement with Biorex by which we acquired our molecular chaperone co-induction drug candidates 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 arimoclomol or any other of these candidates, the milestone payments could aggregate as much as \$3.7 million, with the most significant of those payments due upon the first commercialization of any of these candidates. The actual costs of our planned Phase IIb trial, and any clinical development of arimoclomol in stroke patients, could significantly exceed the expected amount due to a variety of factors associated with the conduct of clinical trials, including those described below under **If Our Products Are Not Successfully Developed and Approved by the FDA, We May Be Forced to Reduce or Curtail Our Operations.**

Under our license for our HIV vaccine candidate, we are responsible for all of the costs for any subsequent clinical trials for this vaccine. The costs of subsequent trials for the HIV vaccine, if initiated, would

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be very substantial. Although we are seeking National Institutes of Health or other governmental funding for these future trials, there can be no assurance that we will be able to secure any such funding. We also will be responsible for milestone payments based upon the development of the vaccine.

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

All of our products in development must be approved by the FDA or foreign governmental agencies before they can be marketed. The process for obtaining FDA and foreign governmental approvals is both time-consuming and costly, with no certainty of a successful outcome. This process typically includes the conduct of extensive pre-clinical and clinical testing, which may take longer or cost more than we or our licensees anticipate, and may prove unsuccessful due to numerous factors. Product candidates that may appear to be promising at early stages of development may not successfully reach the market for a number of reasons. The results of preclinical and initial clinical testing of these products may not necessarily indicate the results that will be obtained from later or more extensive testing. Companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in advanced clinical trials, even after obtaining promising results in earlier trials.

Numerous factors could affect the timing, cost or outcome of our drug development efforts, including the following:

Difficulty in securing centers to conduct trials.

Difficulty in enrolling patients in conformity with required protocols or projected timelines.

Unexpected adverse reactions by patients in trials.

Difficulty in obtaining clinical supplies of the product.

Changes in FDA or foreign governmental 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 foreign governmental 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 revenue from the particular drug candidate.

Our Molecular Chaperone Co-Induction Drug Candidates May Not Receive Regulatory Marketing Approvals

In September 2006, we announced results of our Phase IIa clinical testing of arimoclomol for the treatment of ALS. We reported that arimoclomol had met the trial's primary endpoints of safety and tolerability at all three doses tested in the Phase IIa trial, and that the trial results indicated a non-statistically-significant trend of improvement in functional capacity as measured by the Revised ALS Functional Ration

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Scale in the arimoclomol high dose group as compared with untreated patients. There is no assurance, however, that the results and achievements described will be supported by further analysis of the Phase IIa trial or open-label extension data, or by the results of any subsequent clinical trials, or that the FDA will permit us to commence our planned Phase IIb clinical on a timely basis or at all. The requirements imposed by the FDA in connection with our planned Phase IIb trial could add to the time and expense for us to carry out this trial.

We believe that the FDA may accept the completion of a successful Phase II clinical program as sufficient to enable us to submit a New Drug Application, or NDA; however, there is no assurance that the FDA will accept our Phase II program in lieu of a Phase III clinical trial. If the FDA requires us to complete a Phase III clinical trial, the cost of development of arimoclomol for treatment of ALS will increase significantly beyond our estimated costs, and the time to completion of clinical testing also will be significantly 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. Based upon the positive results of recent preclinical studies in animals, we are considering possible clinical development of arimoclomol in stroke patients. Arimoclomol has also shown therapeutic efficacy in a preclinical animal model of diabetes, and we also may pursue development of arimoclomol for diabetic indications. However, such development would require significant and costly additional testing. There is no guarantee that arimoclomol will show any efficacy for any indication.

Iroxanadine has been tested in two Phase I clinical trials and one Phase II clinical trial which indicated improvement in the function of endothelial cells in blood vessels of patients at risk of cardiovascular disease. We might develop this product 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 licensing it on terms that are attractive to us.

Bimoclomol has been tested in two Phase II clinical trials where it was shown to be safe, but where it did not show efficacy for diabetic neuropathy, the indication for which it was tested. We may 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.

We Recently Identified Material Weaknesses in our Internal Control over Financial Reporting

In our most recent Annual Report on Form 10-K, we reported material weaknesses in the effectiveness of our internal controls over financial reporting related to the application of generally accepted accounting principles arising from our accounting for historical warrant anti-dilution adjustments as deemed dividends, and in the effectiveness of our internal controls over quarterly and annual financial statement reporting arising from our accounting for research and development expenses related to our laboratory facility in Worcester, Massachusetts, which are described in detail under the heading "Controls and Procedures" in our Form 10-K. Despite our substantial efforts to ensure the integrity of our financial reporting process, we cannot guarantee that we will not identify additional weaknesses as we continue to work with the new systems that we have implemented over the past year. Any continuing material weaknesses in our internal control over financial reporting could result in errors in our financial statements, which could erode market confidence in our company, adversely affect the market price of our common stock and, in egregious circumstances, result in possible claims based upon such financial information.

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

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

As a result, these competitors may:

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

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

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

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

Devote greater resources to marketing or selling their products.

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

Introduce products that render our products obsolete.

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

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

Take advantage of other opportunities more readily.

We are aware of only one drug, Rilutek, which was developed by Aventis Pharma AG, that has been approved by the FDA for the treatment of ALS. Rilutek is now available in generic form. Other companies are working to develop pharmaceuticals to treat ALS, including Aeolus Pharmaceuticals, Celgene Corporation, Mitsubishi Pharma Corporation, Ono Pharmaceuticals, Trophos SA, FaustPharmaceuticals SA, Oxford BioMedica plc, and Teva Pharmaceutical Industries Ltd. 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 also 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, Forest Laboratories, Inc., H. Lundbeck A/S, Phytopharm plc, and Schwarz Pharma AG.

A number of products currently are being marketed by a variety of the multinational or other pharmaceutical companies for treating type 2 diabetes, including among others the diabetes drugs Avandia by GlaxoSmithKline PLC, Actos by Eli Lilly & Co., Glucophage and Junavia by Bristol-Myers Squibb Co., Symlin and Byetta by Amylin Pharmaceuticals, Inc. and Starlix by Novartis and the obesity drugs Acomplia

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by Sanofi-Aventis SA, Xenical by F. Hoffman-La Roche Ltd. and Meridia by Abbott Laboratories. Many major pharmaceutical companies are also seeking to develop new therapies for these disease indications. Companies developing HIV vaccines that could compete with our HIV vaccine technology include Merck, GlaxoSmithKline, Sanofi Pasteur, VaxGen, Inc., AlphaVax, Inc. and Immunitor Corporation. These competitors have substantially greater research and product development capabilities and financial, technical, scientific, manufacturing, marketing, distribution and other resources than RXi.

We Will Rely upon Third Parties for the Manufacture of Our Clinical Product Supplies

We do not have the facilities or expertise to manufacture supplies of any of our product candidates, including the clinical supply of arimoclomol used in our Phase II clinical trials. Accordingly, we are dependent upon contract manufacturers or our strategic alliance partners to manufacture these supplies. We have a manufacturing supply arrangement in place with respect to the clinical supplies for the Phase II clinical program for arimoclomol for ALS. We have no manufacturing supply arrangements for any of our other product candidates, and there can be no assurance that we will be able to secure needed manufacturing supply arrangements on attractive terms, or at all. Our failure to secure these arrangements as needed 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 have patents and patent applications directed to our molecular chaperone co-induction technologies, there can be no assurance that these patents and applications will 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 related to our molecular chaperone co-induction drug candidates, and received certain representations and warranties from the seller in connection with the acquisition, the patents and patent applications related to our molecular chaperone co-induction drug candidates 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.

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

We Are Subject to Potential Liabilities From Clinical Testing and Future 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 obtained clinical trial insurance for our Phase IIa clinical trial of arimoclomol for the treatment of ALS, and will seek to obtain similar insurance for the planned Phase IIb clinical trial of arimoclomol and any other clinical trials that we conduct, as well as liability insurance for any products that we market. 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. There is no assurance, however, that

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any insurance maintained by us or our licensees will prove adequate in the event of a claim against us. Even if claims asserted against us are unsuccessful, they may divert management's attention from our operations and we may have to incur substantial costs to defend such claims.

We May Be Unable to Acquire Products Approved For Marketing

In the future, we may seek to acquire products from third parties that already are being marketed or have been approved for marketing. We have not identified any of these products, and we do not have any prior experience in acquiring or marketing products and may need to find third parties to market any products that we might acquire. 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.

Risks Associated With Our Ownership of RXi

The value of our ownership interest in RXi will depend upon RXi's success in developing and commercializing products based upon its RNAi technologies, which is subject to significant risks and uncertainties, including the following:

RXi is Subject to Risks of a New Business

RXi is a start-up company with no operating history. RXi initially will focus solely on developing and commercializing therapeutic products based upon its RNAi technologies, and there is no assurance that RXi will be able to successfully implement its business plan. While RXi's management collectively possesses substantial business experience, including experience in taking start-up companies from early stage to an operational stage, there is no assurance that they will be able to manage RXi's business effectively, or that they will be able to identify, hire and retain any needed additional management or scientific personnel, to develop and implement RXi's product development plans, obtain third-party contracts or any needed financing, or achieve the other components of RXi's business plan.

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

The RNAi technologies that RXi has licensed from UMMS have not yet been clinically tested by CytRx or RXi, nor are we aware of any clinical trials having been completed by third parties involving similar technologies. The scientific discoveries that form the basis for RXi's 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, and no company has received regulatory approval to market therapeutics utilizing RNAi. Successful development of RNAi-based products by RXi 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. RXi may expend large amounts of money trying to solve these issues, and never succeed in doing so. In addition, any compounds that RXi develops 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 even harmful ways.

RXi May Be Unable to Protect Its Intellectual Property Rights Licensed From UMMS or May Need to License Additional Intellectual Property from Others.

The assets we contributed to RXi include a non-exclusive license to the fundamental Fire and Mello patent owned by UMMS and the Carnegie Institution of Washington, which claims various aspects of gene silencing, or genetic inhibition by double-stranded RNA. There can be no assurance that this patent or other pending applications or issued patents belonging to its patent family would withstand possible legal challenges or that it will effectively insulate the covered technologies from competition. Therapeutic applications of gene

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silencing technology and other technologies that RXi licenses from UMMS are also claimed in a number of UMMS pending patent applications, but there can be no assurance that these applications will result in any issued patents or that any such issued patents would withstand possible legal challenges or insulate RXi's technologies from competition. We are aware of a number of third party-issued patents directed to various particular forms and compositions of RNAi-mediating molecules, and therapeutic methods using them, that RXi will not use. Third parties may, however, hold or seek to obtain additional patents that could make it more difficult or impossible for RXi to develop products based on the gene silencing technology that RXi has licensed.

RXi has entered into an invention disclosure agreement with UMMS under which UMMS has agreed to disclose to RXi certain inventions it makes and give RXi the exclusive right to negotiate licenses to the disclosed inventions. There can be no assurance, however, that any such inventions will arise, that RXi will be able to negotiate licenses to any inventions on satisfactory terms, or at all, or that any negotiated licenses will prove commercially successful.

RXi may need to license additional intellectual property rights from third parties in order to be able to complete the development or enhance the efficacy of its product candidates or avoid possible infringement of the rights of others. There is no assurance that RXi will be able to acquire any additional intellectual property rights on satisfactory terms, or at all.

We Are Required To Dispose of Some of Our RXi Shares, and May Not Be Able To Do So Promptly Through the Issuance of a Dividend

We have agreed under our letter agreement with UMMS and our separate stockholders agreement with RXi and its other current stockholders to reduce our share of ownership of RXi to less than a majority of the outstanding voting power as soon as reasonably practicable. In order to do so, we intend to make a dividend or distribution of a portion of our RXi shares to our stockholders. Any future dividend or other distribution to our stockholders of RXi shares would be subject to the approval of our board of directors and to compliance with SEC rules and the requirements of the Delaware General Corporation Law, and there is no assurance as to the timing or amount of such dividend or distribution. We may be unable to comply with these rules and requirements, or may experience delays in complying. Any such dividend or distribution would likely be taxable to our stockholders.

RXi May Not Be Able to Obtain Future Financing

On April 30, 2007, we provided to RXi \$15.0 million, net of approximately \$2.0 million of expenses reimbursed to us by RXi, to satisfy the initial funding requirements under its agreements with UMMS. We believe this initial funding will be sufficient to fund RXi's planned business and operations into the third quarter of 2008. It is possible, however, that RXi could require additional funding prior to this time. RXi also will require substantial additional financing in the future in connection with its RNAi research and development activities and any commercialization of its products. We contributed all of our RNAi-related technologies to RXi in order to accelerate the development and commercialization of drugs based upon these and RXi's other RNAi technologies. Although we believe that this will facilitate obtaining additional financing to pursue RXi's RNAi development efforts, RXi has no commitments or arrangements for any financing, and there is no assurance that it will be able to obtain any future financing.

We May Not be Able to Exercise Our RXi Preemptive Rights

Under our agreement with RXi and its other current stockholders, with some exceptions, once we no longer own a majority of RXi's outstanding shares CytRx will have preemptive rights to acquire a portion of any new securities sold or issued by RXi so as to maintain our percentage ownership of RXi. Depending upon the terms and provisions of any proposed sale of new securities by RXi, we may be unable or unwilling to exercise our preemptive rights, in which event our percentage ownership of RXi will be diluted. In order to

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maintain our percentage ownership of RXi, we may need to obtain our own financing, which may or may not be available to us on satisfactory terms, or at all.

RXi Retains Discretion Over Its Use of Any Funds That We Provide To It

Although RXi currently is a majority-owned subsidiary of ours, we do not control its day-to-day operations. Accordingly, all funds received by RXi, including funds provided by us, may be used by RXi in any manner its management deems appropriate, for its own purposes, including the payment of salaries and expenses of its officers and other employees, amounts called for under the UMMS licenses and invention disclosure agreement, and for other costs and expenses of its RNAi research and development activities.

We Do Not Control RXi, And The Officers, Directors and Other RXi Stockholders May Have Interests That Are Different From Ours

We have entered into a letter agreement with UMMS and a separate agreement with RXi and its other current stockholders under which we agree during the term of RXi's new licenses from UMMS to vote our shares of RXi common stock for the election of directors of RXi and to take other actions to ensure that a majority of the RXi board of directors are independent of us. We also have agreed that we will reduce our ownership to less than a majority as soon as reasonably practicable. At any time at which we own less than a majority of the voting power RXi, we will not be able to determine the outcome of matters submitted to a vote of RXi stockholders. The other stockholders of RXi also may have interests that are different from ours. Accordingly, RXi may engage in actions or develop its business and operations in a manner that we believe are not in our best interests.

Products Developed by RXi Could Eventually Compete With Our Products For ALS, Type 2 Diabetes and Obesity and Other Disease Indications

RXi has determined to focus its initial efforts on developing an RNAi therapeutics for the treatment of a specific form of ALS caused by a defect in the SOD1 gene. Although arimoclomol is being developed by CytRx for all forms of ALS, it is possible that any products developed by RXi for the treatment of ALS could compete with any ALS products that CytRx may develop. RXi also plans to pursue the development of RNAi therapeutics for the treatment of obesity and type 2 diabetes, which could compete with any products that CytRx may develop for the treatment of these diseases. The potential commercial success of any products that CytRx may develop for these and other diseases may be adversely effected by competing products that RXi may develop.

RXi Will Be Subject to Competition, and It May Not Be Able To Compete Successfully

A number of medical institutions and pharmaceutical companies are seeking to develop products based on gene silencing technologies. Companies working in this area include Alnylam Pharmaceuticals, Sirna Therapeutics (which was recently acquired by Merck), Acuity Pharmaceuticals, Natestch Pharmaceutical Company Inc., Nucleonics, Inc., Tacere Therapeutics Inc. and Benitec Ltd. and a number of the multinational pharmaceutical companies. These competitors have substantially greater research and development capabilities and financial, scientific, technical, manufacturing, marketing, distribution, and other resources than RXi, and RXi may not be able to compete successfully.

Risks Associated with Our Common Stock

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

We have a stockholder rights plan and provisions in our bylaws that may discourage or prevent a person or group from acquiring us without the participation and approval of our board of directors. We recently extended the stockholder rights plan through April 2017.

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

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

As of April 30, 2007, there were outstanding stock options and warrants to purchase approximately 22.4 million shares of our common stock at a weighted-average exercise price of \$1.87 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. Many of our outstanding warrants contain anti-dilution provisions pertaining to dividends or distributions with respect to our common stock that could be triggered upon our intended dividend or distribution of RXi shares. Our outstanding warrants to purchase approximately 1.4 million shares also contain anti-dilution provisions that are triggered upon any issuance of securities by us below the prevailing market price of our common stock. In the event that these anti-dilution provisions are triggered by us in the future, we would be required to reduce the exercise price, and increase the number of shares underlying, those warrants, which would have a dilutive effect on our stockholders.

As of April 30, 2007, we had registered with the SEC for resale by our stockholders a total of approximately 59.9 million outstanding shares of our common stock, including the 8,765,000 shares being offered under this prospectus, and approximately 22.4 million additional shares of our common stock issuable upon exercise of outstanding options and warrants. The availability of these shares for public resale, as well as actual resales 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

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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.

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

The market price of our common stock has ranged from \$0.87 to \$5.49 per share during the 52-week period ended April 30, 2007, and may continue to experience significant volatility from time to time. Factors such as the following may affect such volatility:

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

Changes in our relationship with our licensors and other strategic partners=.

Changes in our ownership or other relationships with RXi.

Our quarterly operating results.

Developments in patent or other technology ownership rights.

Public concern regarding the safety of our products.

Government regulation of drug pricing.

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

USE OF PROCEEDS

The selling stockholders will receive all of the proceeds from the sale of shares under this prospectus. We will not receive any proceeds from the sale of the shares by the selling stockholders. We will bear the costs and expenses of this offering, except that the selling stockholders will bear any commissions and discounts attributable to their sale of the shares.

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

	Sale Price	
	High	Low
2007		
Second Quarter (through April 30, 2007)	\$5.36	\$4.07
First Quarter	5.49	1.74
2006		
Fourth Quarter	\$2.04	\$1.21
Third Quarter	1.94	0.87
Second Quarter	2.30	1.06
First Quarter	1.92	1.01
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

Holder

On April 30, 2007, there were approximately 8,800 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.

Dividends

We have not paid any dividends since our inception and do not contemplate paying any cash dividends in the foreseeable future.

ABOUT CYTRX**General**

CytRx is a biopharmaceutical research and development company engaged in developing human therapeutic products based primarily upon our small molecule molecular chaperone co-induction technology. We recently completed a Phase IIa clinical trial of our lead small molecule product candidate, arimoclomol, for the treatment of amyotrophic lateral sclerosis, which is commonly known as ALS or Lou Gehrig's disease. Arimoclomol has received Orphan Drug and Fast Track designation from the FDA and orphan medicinal product status from the European Commission for the treatment of ALS. We plan to initiate a Phase IIb trial of arimoclomol for this indication during the second half of 2007, subject to FDA clearance. Recent preclinical animal studies indicated that arimoclomol accelerated the recovery of sensory and motor functions following a stroke, even when administered up to 48 hours after the stroke. Based upon the positive results of these studies, we are considering a possible phase II clinical trial of arimoclomol in stroke patients. We also are pursuing clinical development of our other small molecule product candidates, as well as 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 with funding from the National Institutes of Health. We have previously entered into strategic alliances with respect to the development of products using our other technologies.

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In October 2004, we acquired all of the clinical and pharmaceutical and related intellectual property assets of Biorex Research & Development, RT, a Hungarian company, which we refer to as Biorex. The Biorex assets consist primarily of arimoclomol and other novel small molecules based on molecular chaperone co-induction technology, which we believe may have broad therapeutic applications in neurology, type 2 diabetes, cardiology and diabetic complications. These assets also included two other oral, clinical stage drug candidates and a library of small molecule product candidates.

We also are engaged through RXi Pharmaceuticals Corporation, our majority-owned subsidiary, in developing therapeutic products based upon RNAi, which has the potential to effectively treat a broad array of diseases by interfering with the expression of targeted disease-associated genes. RXi will focus solely on developing and commercializing therapeutic products based upon RNAi technologies for the treatment of human diseases, with an initial focus on neurodegenerative diseases, cancer, type 2 diabetes and obesity. See RXi Pharmaceuticals Corporation below for a description of the technologies, research and development activities and current business plan of RXi.

Molecular Chaperone Co-Induction Platform

The synthesis of proteins is a normal part of essential human cell activity. Proteins are linear chains of amino acids. In order to function normally in a cell, these proteins must fold into particular three-dimensional shapes. During stressful conditions such as certain disease states, proteins can fold improperly, resulting in aggregation of protein that can be toxic to the cell. It is believed, for example, that mis-folding and aggregation of certain mutated forms of a particular protein known as superoxide dismutase 1, or SOD1, leads to the death of motor neurons that causes certain forms of ALS.

In nature, the cell has developed chaperone proteins to deal with these potentially toxic mis-folded proteins. Chaperones are a key component of the human body's universal cellular protection, maintenance and repair mechanism. They help to ensure that newly synthesized proteins are complete, situated correctly 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. 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 within the human body.

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 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, now more commonly referred to as the stress response, increases the synthesis of molecular chaperones that then repair or degrade the mis-folded proteins.

The stress response can be an important mechanism for cellular survival during certain acute physical stresses. For instance, prior induction of the stress response can protect tissue culture cells from heat-induced cell death. It appears, however, 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 such as ALS may be slowed, halted or perhaps even reversed. In test tube experiments, mammalian cells engineered to have increased amounts of molecular chaperones have been shown to be resistant to a variety of otherwise lethal stresses. In animal studies, genetically engineered mice with 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

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bulbar muscular atrophy. We believe that these scientific studies support the possibility that drugs such as arimoclomol may be capable of boosting the stress response in humans.

Among the assets that we acquired from Biorex are several drug candidates whose mechanism of action is believed to be the co-induction of the stress response; meaning that they amplify the production of molecular chaperone proteins that are already activated by disease-induced cellular stress, but do not seem to activate the stress response by themselves. In doing so, the drug candidates may selectively amplify molecular chaperone proteins specifically in diseased tissue, which may minimize potential drug side-effects. If confirmed, this amplification of the cell's own fundamental protective mechanism may have powerful therapeutic and prophylactic potential in a broad array of medical applications.

We believe that our molecular chaperone co-induction drug candidates can potentially improve the cell's natural ability to resist the toxic effects of protein mis-folding caused by both acute and chronic diseases. These orally available small molecule drug candidates may accomplish some of the same goals as RNAi described below, but would do so by a mechanism of repairing or degrading the offending proteins, instead of degrading their corresponding messenger RNA, or mRNAs. Since the ability to recognize mis-folded proteins is an intrinsic feature of the amplified molecular chaperones, molecular chaperone therapy may not require identifying the actual molecular target of the stress-induced damage. As a result, these product candidates may have broader therapeutic utility for the removal of damaged proteins compared to that of RNAi, which requires identifying the actual mis-folded proteins.

We are not aware of another pharmaceutical company engaged in developing small molecule co-inducers of molecular chaperones. At least a few potential drug candidates have been reported in scientific papers as activating molecular chaperone expression, but they appear to activate stress response in all cells rather than to amplify the cell's own protective mechanisms that are activated only in stressed or diseased cells.

Product Development***ALS Clinical Trials***

We are pursuing directly and indirectly through RXi the development of therapeutics for the treatment of various forms of ALS. 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. Worldwide, approximately 120,000 people are living with ALS.

We recently completed the initial Phase II clinical trial, which we refer to as the Phase IIa trial, for arimoclomol for ALS. The Phase IIa trial was a multicenter, double-blind, placebo-controlled study of approximately 80 ALS patients enrolled at ten clinical centers across the U.S. Patients received either a placebo in the form of a capsule without drug, or one of three dose levels of arimoclomol capsules three times daily for a period of 12 weeks, immediately followed by a one-month period without the drug. The primary endpoints of this Phase IIa trial were safety and tolerability. Secondary endpoints included a preliminary evaluation of efficacy using two widely accepted surrogate markers, the revised ALS Functional Rating Scale, or ALSFRS-R, which is used to determine patients' capacity and independence in 13 functional activities, and Vital Capacity, or VC, an assessment of lung capacity. The trial was designed to monitor only extreme responses in these two categories. We have extended the initial Phase IIa trial on an open-label basis, meaning that the medication was no longer blinded to the patients or their doctors, in order to provide additional data regarding safety and tolerability. As a result, approximately 70 patients who completed the Phase IIa study and who met the eligibility criteria received arimoclomol at the highest investigative dose for up to an additional six months. We expect the results of this open-label extension to be available in the second quarter of 2007.

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We are encouraged by the results of our recently completed Phase IIa clinical trial of arimoclomol for the treatment of ALS, which appeared to be safe and well tolerated by the patients in that trial even at the highest administered dose. Arimoclomol also was found to effectively enter the cerebral spinal fluid, demonstrating that it passed the blood:brain barrier. We plan to determine the highest dose that can be well tolerated in healthy volunteers in a multiple ascending dose study, and then plan to initiate a subsequent Phase II trial, which we refer to as the Phase IIb trial, that will be designed to detect more subtle efficacy responses. On February 5, 2007, we entered into with Pharmaceutical Research Associates, or PRA, a Master Agreement for Clinical Trials Management Services under which PRA will provide clinical research services in connection with the design, management and conduct of both the multiple ascending dose study and the Phase IIb clinical trial. Although the Phase IIb efficacy trial is still in the planning stages and will be subject to FDA clearance, at present we expect it to include approximately 400 ALS patients recruited from 30-35 clinical sites to take approximately 18 months after initiation to complete. Our agreement with PRA is part of our business plan to pursue our product development efforts primarily by contract with clinical research companies and other third parties.

Obesity and Type 2 Diabetes

Obesity and type 2 diabetes are major 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.

One of our product candidates, irovanadine, was shown to be well tolerated and demonstrated significant improvement of vascular function in the brachial artery of hypertensive patients in Phase I and Phase II clinical trials conducted prior to our acquisition of irovanadine. We intend to evaluate the preclinical efficacy of this product candidate for diabetic complications, including wound healing. If this compound proves to be efficacious in preclinical work, we would consider initiation of a Phase II clinical trial for one of these indications.

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

Stroke Recovery

CytRx recently announced additional data indicating that arimoclomol improved functional recovery in experimental animal models of stroke. In these additional preclinical animal studies, arimoclomol significantly accelerated the recovery of sensory and motor functions, even when administered up to 48 hours after the stroke. These data suggest that arimoclomol can accelerate the repair of the neurological damage caused by stroke. Based upon these animal studies, we are considering a possible phase II clinical trial of arimoclomol in stroke patients. It is possible that the large therapeutic window for administering arimoclomol in animals could simplify patient enrollment in clinical trials compared to other stroke studies.

Cardiovascular Disease

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

Table of Contents***HIV***

Our HIV subunit vaccine technology 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, or agent to increase effectiveness, 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 promising Phase I clinical trial results that indicate its ability to produce potent antibody responses with neutralizing activity against multiple HIV viral strains, and we are continuing to analyze the Phase I results to determine how, or if, to proceed with clinical development. 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.

Other Technologies and Strategic Arrangements

Our other primary technologies, which we acquired or developed prior to the acquisition of our molecular chaperone technology, are CRL-5861, an intravenous agent for treatment of sickle cell disease and other acute vaso-occlusive disorders, and TranzFect, a delivery technology for DNA and conventional-based vaccines. In October 2003, we entered into a strategic relationship with another entity to complete the development of CRL-5861. We have licensed our TranzFect technology to two other companies. We may also seek to license this technology as a potential conventional adjuvant for hepatitis C, human papilloma virus, herpes simplex virus and other viral diseases or for use as a non-clinical research reagent to increase transfection *in vitro* or in laboratory animals. Adjuvants are agents added to a vaccine to increase its effectiveness.

Therapeutic Copolymer Program

CRL-5861 (purified poloxamer 188) is an intravenous agent for the treatment of sickle cell disease and other acute vaso-occlusive disorders. Sickle cell disease is an inherited disease caused by a genetic mutation of hemoglobin in the blood, and acute vaso-occlusive disorders are a blockage of blood flow caused by deformed, or sickled, red blood cells which can cause intense pain in sickle cell disease patients. In June 2004, we licensed our copolymer technologies, including CRL-5861, on an exclusive basis, to SynthRx, Inc., a Houston, Texas-based biopharmaceutical company, in exchange for a cash payment and ownership interest in SynthRx. Upon commercialization of any products developed under our alliance with SynthRx, we may also receive milestone payments and royalties.

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. The limited revenues that we generated prior to 2006 have been due primarily to license fees paid to us with respect to our TranzFect technology, which represented 54% and 93% of our total revenues for the years ended December 31, 2005 and 2004, respectively.

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Merck License

In November 2000, we entered into an exclusive, worldwide license agreement with Merck & Co., Inc. under which we granted Merck the right to use our TranzFect technology in DNA-based vaccines for HIV and three other targets. In July 2003, Merck returned to us the rights to the three other targets covered by its license, which we are able to license to other third parties. Merck has 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.

Vical License

We are party to a license agreement with Vical Incorporated under which we grant to 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 the four targets previously licensed by us to Merck, DNA vaccines or therapeutics based on prostate-specific membrane antigen, or PSMA, and 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 are entitled to receive milestone and royalty payments in the future based on criteria described in the agreement.

ABOUT RXI

General

Our board of directors periodically reviews and assesses strategic alternatives for our company, and determined that the best strategy for realizing the potential value of our RNAi technologies was to create a subsidiary focused on RNAi therapeutics. RXi, our RNAi therapeutics subsidiary, was formed by CytRx and four leading RNAi researchers, including Craig C. Mello, Ph.D., who was awarded the 2006 Nobel Prize in Medicine for his co-discovery of RNAi. Any such dividend or distribution also would likely be taxable to our stockholders. In January 2007, we transferred to RXi substantially all of our RNAi-related technologies and assets in exchange for equity in RXi. These technologies and assets consisted primarily of our licenses from UMMS and the Carnegie Institution of Washington relating to fundamental RNAi technologies, as well as research and other equipment situated at our Worcester, Massachusetts laboratory. To date, RXi's principal activities have consisted of acquiring our RNAi-related assets, entering into four new RNAi technology licenses and an invention disclosure agreement with UMMS, developing research and clinical development plans for its RNAi therapeutic platform, assessing and negotiating licenses to additional therapeutic RNAi technology, recruiting a RNAi-focused management and scientific/clinical advisory team and completing its organizational activities.

RXi Agreements and Arrangements

We have entered into the following agreements and arrangements relating to RXi:

Contribution Agreement

On January 8, 2007, we entered into a Contribution Agreement with RXi under which we assigned and contributed to RXi substantially all of our RNAi-related technologies and assets. The assigned technologies and assets consisted primarily of our licenses from UMMS and from the Carnegie Institution of Washington relating to fundamental RNAi technologies, as well as equipment situated at our Worcester,

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Massachusetts, laboratory. The licensed technologies include patent applications on RNAi target sequences, chemical modifications and delivery to cells, field-specific licenses to a patent application on chemical modification of RNAi invented by Tariq M. Rana, Ph.D., the Tuschl I patent, and our exclusive licenses to patent applications that disclose gene targets for diabetes and obesity, including RIP140 (see, Material Licenses and Other Agreements, below). In connection with the contribution of the licenses and other assets, RXi assumed primary responsibility for all payments to UMMS and other obligations under the contributed licenses and assets.

Voting Agreement

As part of our new business strategy, RXi began operating as a stand-alone company in January 2007 and is focused solely on developing and commercializing therapeutic products based upon RNAi technologies for the treatment of human diseases. In order to facilitate this strategy, and as an inducement to UMMS to enter the new licenses and the invention disclosure agreement with RXi described below under Material Licenses and Other Agreements, on January 10, 2007, we entered into a letter agreement with UMMS regarding the management of RXi. Under the letter agreement, we have agreed that, during the term of our new UMMS licenses, we will vote our shares of RXi common stock for the election of directors of RXi and take other actions to ensure that a majority of the RXi board of directors are independent of CytRx.

We have agreed in the letter agreement that we will reduce our ownership interest in RXi's capital stock to less than a majority as soon as reasonably practicable. In order to do so, we intend to make a dividend or distribution of a portion of our RXi shares to our stockholders. Any future dividend or other distribution to our stockholders of RXi shares would be subject to the approval of our board of directors and to compliance with SEC rules and the requirements of the Delaware General Corporation Law, and there is no assurance as to the timing or amount of such dividend or distribution. Any such dividend or distribution would likely be taxable to our stockholders.

Stockholder and Preemptive Rights Agreement

On February 23, 2007, we entered into a letter agreement with RXi and the other current stockholders of RXi. Under the stockholders agreement, RXi has agreed to grant to CytRx preemptive rights to acquire any new securities (as defined) that RXi proposes to sell or issue so that we may maintain our percentage ownership of RXi. The preemptive rights will become effective if CytRx owns at any time less than 50% of the outstanding shares of RXi common stock, and will expire on January 8, 2012, or such earlier time at which CytRx owns less than 10% of the outstanding RXi common stock.

Under the stockholders agreement, we also undertake to vote our shares of RXi stock in the election of directors of RXi and dispose of our RXi shares in accordance with the terms of our letter agreement with UMMS described above. We have further agreed in the stockholders agreement to approve of actions that may be adopted and recommended by RXi's board of directors to facilitate any future financing of RXi.

Completion of RXi's Initial Funding

On April 30, 2007, we entered into a Contribution Agreement with RXi, pursuant to which we contributed to RXi \$17.0 million in order to satisfy RXi's initial funding requirements under its various agreements with UMMS. In exchange for the contribution, RXi issued to CytRx shares of common stock of RXi sufficient to increase CytRx's ownership to approximately 89.4% of the outstanding RXi shares. CytRx's percentage ownership does not give effect to any shares to be issued to UMMS by RXi as described below. RXi used a portion of the initial funding provided by CytRx to reimburse CytRx approximately \$2.0 million of estimated organizational and operational expenses incurred by us in connection with the formation, initial operations and funding of RXi.

Table of Contents***Reimbursement Agreement***

As of January 8, 2007, we entered into a letter agreement with RXi under which RXi agreed to reimburse us following its initial funding for all organizational and operational expenses incurred by us in connection with the formation, initial operations and funding of RXi. As of March 31, 2007, we had advanced approximately \$2.0 million to RXi for which we have since been reimbursed by RXI. We have no commitment or understanding to provide any additional funds to RXi.

RNAi Therapeutic Platform

RNAi technology uses short double-stranded RNA, or dsRNA, molecules to silence targeted genes and, as a result, is commonly referred to as gene silencing. RNAi has been shown to effectively silence targeted genes within living cells with great specificity and potency. As a result, RNAi technology may effectively silence targeted genes without impacting other, non-targeted, genes. RNAi is regarded as a significant advancement in gene silencing and was featured in *Science* magazine as the Breakthrough of the Year in 2002.

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 offers a novel approach to the drug development process that can target any one of the genes in the human genome. In contrast, only a small subset of the proteins encoded in the genome can be targeted by traditional medicinal chemistry or antibody based approaches. The specificity of RNAi is achieved via a well-understood biological mechanism based on matching the sequence of an RNAi to the sequence of the targeted gene. The specificity of RNAi may be sufficient to permit therapeutic targeting of only a single gene or even the mutant form of a gene. The ability to specifically target mutant forms of a gene is critical in many diseases, such as cancer and neurodegenerative disorders, where spontaneous or inherited changes in otherwise necessary genes are the underlying cause of disease.

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). Within the cell, dsRNA is thought to 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.

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 five clinical trials using RNAi,

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namely trials for age-related macular degeneration by Acuity Pharmaceuticals, Allergan Inc. and Quark Biotech Inc., for respiratory syncytial virus by Alnylam Pharmaceuticals and for diabetic macular edema by Acuity Pharmaceuticals.

RXi has determined that the initial indication that it plans to pursue is a form of ALS caused by a defect in the SOD1 gene. Early preclinical studies in a mouse model of SOD1 mediated ALS conducted by Dr. Tariq Rana of UMMS, one of RXi's scientific founders and a member of our scientific advisory board and Dr. Zuoshang Xu of UMMS showed promising results using an RNAi therapeutic to inhibit the defective SOD1 gene. RXi's second planned indication is the treatment of obesity and type 2 diabetes. RXi has in-licensed intellectual property regarding the RIP140 gene, which appears to be an important regulator of metabolism, and may target this gene in future therapeutic product development programs.

Although RXi's near-term focus will be on ALS and type 2 diabetes, RXi plans to leverage its experience related to local delivery of RNAi therapeutics to seek to develop RNAi-based treatments for neurodegenerative diseases other than ALS. For example, in addition to ALS, many neurodegenerative diseases exist for which no effective therapies are available, including Alzheimers, Huntington's and Parkinson's diseases. In many of these cases, molecular targets have been identified that are difficult to access by conventional small molecule or antibody based approaches. RXi believes that the knowledge gained in its discovery and development activities related to ALS will allow RXi to rapidly move into additional related therapeutic areas.

RXi may also pursue preclinical studies in several additional disease areas, with the goal of creating multiple clinical development programs. For example, RXi founding scientist Greg Hannon, Ph.D. is a leader in the understanding of tumor-suppressor and oncogene pathways, and RXi expects that Dr. Hannon's involvement with RXi will provide insight into potential cancer therapeutic targets. Many well-studied targets exist for numerous diseases that RXi believes will be difficult to target with normal medicinal chemistry. RXi will focus on combining its expertise in RNAi with existing disease models through collaborative interactions with academic, biotech and pharmaceutical industry scientists.

Material Licenses and Other Agreements

License Agreements

Through our initial strategic alliance with UMMS that we initiated in 2003, we acquired the rights to a portfolio of technologies, including the rights to use UMMS's proprietary RNAi technology as a potential therapeutic in certain defined areas that include obesity, type 2 diabetes, ALS and cytomegalovirus, or CMV, and in the identification and screening of novel protein targets. Pursuant to the Contribution Agreement that we entered into with RXi on January 8, 2007, we assigned those rights to RXi.

In addition to the RNAi licenses and rights that we contributed to RXi, on January 10, 2007, RXi entered into three exclusive, worldwide, sublicenseable licenses with UMMS for three different patent families and one non-exclusive, worldwide, non-sublicenseable license for a fourth patent family, which we refer to collectively as the 2007 UMMS licenses, pursuant to which UMMS granted RXi rights under certain UMMS patent applications to make, use and sell products related to applications of RNAi technologies. The 2007 UMMS licenses include an exclusive license covering nanotransporters, which may be effective in the delivery of RNAi compounds, as well as methods and potential compounds for the potential treatment of ALS that can be delivered locally to the central nervous system.

As consideration for the 2007 UMMS licenses, we paid UMMS an aggregate up-front fee of \$75,000 and reimbursed UMMS \$103,000 for previously incurred patent expenses. Following the completion of RXi's initial funding, RXi will pay UMMS an additional license fee of \$175,000 and issue to UMMS an aggregate of \$1,600,000 of RXi common stock that was valued on a per-share basis for this purpose based on the valuation of RXi in its initial funding. The valuation of RXi for this purpose does not necessarily bear any relationship to the actual present or potential future value of RXi.

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The foregoing license agreements with UMMS require us to make aggregate payments of up to \$300,000 in 2007. In subsequent periods, we will be required to make aggregate payments ranging from \$250,000 to \$1.7 million per year to maintain the licenses through 2018. We are obligated to pay legal expenses for the prosecution of patents licensed from UMMS, which we anticipate will be approximately \$175,000 during 2007, and to make milestone payments to UMMS based upon our progress in the clinical development and marketing of products utilizing the technologies licensed from UMMS. In the event that we were to successfully develop a product in each of the categories of obesity/type 2 diabetes and ALS, these milestone payments could aggregate up to \$27.4 million. We do not anticipate the occurrence of an event that would require a milestone payment during 2007. We also would be required to pay royalties to UMMS based on the net sales of those products. The actual milestone payments will vary, perhaps significantly, based upon the milestones we achieve and the products, if any, we develop.

New Invention Disclosure Agreement

On January 10, 2007, RXi also entered into an invention disclosure agreement with UMMS pursuant to which UMMS is obligated for a three-year period to disclose to RXi any unrestricted inventions conceived or reduced to practice by UMMS related to therapeutic applications of RNAi technologies. Under the invention disclosure agreement, UMMS also grants to RXi an option to negotiate the terms of a license to any disclosed inventions. If RXi exercises the option and the parties are unable to reach agreement on the terms of any such license, RXi may elect to have an arbitrator determine the terms of the license. RXi will pay UMMS \$100,000 in cash and issue to UMMS \$800,000 of RXi common stock that will be valued on a per-share basis for this purpose based on the valuation of RXi in its initial funding. We are obligated to pay UMMS \$100,000 on each of April 30, 2008 and 2009. RXi also will be obligated to pay UMMS a fee each time RXi exercises its right to negotiate a license under the invention disclosure agreement. The invention disclosure agreement is terminable by RXi or UMMS upon an uncured breach by the other party, and RXi may terminate the agreement at any time for any reason.

Patents and Proprietary Technology***CytRx Corporation***

We actively seek patent protection for our technologies, processes, uses, and ongoing improvements and consider our patents and other intellectual property to be critical to our business. We acquired patents and patent applications, and have filed several new patent applications, in connection with our molecular chaperone program, and we have licensed additional technologies, including patents or patent applications, most of which are in the RNAi field.

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

In addition to patent protection, we attempt to protect our proprietary products, processes and other information by relying on trade secrets and non-disclosure agreements with our employees, consultants and certain other persons who have access to such products, processes and information. Under the agreements, all inventions conceived by employees are our exclusive property, but there is no assurance that these agreements

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will afford significant protection against misappropriation or unauthorized disclosure of our trade secrets and confidential information.

RXi Pharmaceuticals Corporation

RXi has secured exclusive and non-exclusive rights to develop RNAi therapeutics by licensing key RNAi technologies and patent rights. The patents, patent applications and exclusive rights to intellectual property rights are directed to key therapeutic targets, chemistry and configurations of RNAi and delivery of RNAi within the body in a therapeutically effective manner.

Intellectual Property Rights to Key Therapeutic Targets

RXi's portfolio of licenses from UMMS consist of certain inventions and technologies developed primarily by Drs. Craig Mello, Michael Czech and Tariq Rana directed to RXi's key therapeutic areas. These areas are: genetic diseases involving a dominant mutation (such as ALS); disorders and diseases of metabolic control such as diabetes and obesity; and infectious agent related diseases such as disorders related to CMV.

RXi has an exclusive license from UMMS to technology, patents and pending patent applications directed to the design and synthesis of chemically modified RNAi, and *in vivo* methods using RNAi to treat allele-specific genetic diseases such as ALS.

RXi also has an exclusive license from UMMS to technology, patents and pending patent applications directed to RNAi that targets RIP140, a co-repressor of many nuclear receptors and a key factor involved in sugar uptake and oxidative metabolism, and consequently, diabetes and obesity. RXi is an exclusive licensee of UMMS's technology establishing the key role of RIP140 in diabetes and insulin action. RXi is also entitled to obtain first rights to cellular targets involved in diabetes and obesity as they are identified in Dr. Czech's laboratory at UMMS. In addition, RXi has rights to technology, patents and pending patent applications directed to the use of the endoplasmic reticulum stress response pathway in adipose cells to enhance whole body insulin sensitivity.

RNAi based therapeutics may be used to combat infectious diseases, especially viral diseases. RXi has exclusive rights from UMMS to technology, patents and pending patent applications directed to treatment of CMV-related disorders using RNAi.

Intellectual Property Rights to Chemistry and Configurations of Therapeutically Useful RNAi

In addition to a non-exclusive license to Dr. Andrew Fire's and Dr. Mello's foundational patent covering the use of dsRNA to induce gene silencing, RXi has secured exclusive and co-exclusive rights from UMMS to technologies, patents and pending patent applications related to fundamental technologies with the potential to produce stable and therapeutically effective RNAi therapeutics in the key areas of RXi's business focus, which are ALS, diabetes, obesity, and conditions associated with CMV infection. These licensed technologies include:

Dr. Tariq Rana's inventions regarding the fundamental rules of designing chemically-modified RNAi sequences that are suitable for *in vivo* gene silencing;

Dr. Tuschl's invention regarding RNAi therapeutics using double-stranded RNAs of 19 to 23 nucleotides; and

Drs. Mello and Zamore's invention regarding *in vivo* production of siRNA.

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Intellectual Property Rights to Delivery of RNAi to Cells

RXi also has obtained exclusive and non-exclusive licenses to technologies potentially necessary for the efficient delivery of RNAi therapeutics to cells *in vitro* and *in vivo*. These technologies include:

methods and compositions, including use of nanotransporters, for efficient RNAi delivery for therapeutic gene silencing in cells and animals; and

inhibition of gene expression in adipocytes using RNAi.

Beneficial Ownership of RXi's Securities

As of May 1, 2007, RXi had outstanding 6,703 shares of common stock, of which 5,991 shares were owned by CytRx. The remaining RXi shares outstanding as of May 1, 2007 were owned by the current members of RXi's scientific advisory board.

SELLING STOCKHOLDERS

On April 19, 2007, we sold 8,615,000 shares of our common stock to the selling stockholders pursuant to a purchase agreement under which we agreed to file with the SEC by May 4, 2007 a registration statement with respect to the resale of the shares by the selling stockholders. We agreed in the purchase agreement to use our reasonable efforts to cause the registration statement to be declared effective under the Securities Act not later than June 18, 2007. The registration statement of which this prospectus is a part is intended to satisfy these obligations. We further agreed, subject to some exceptions, to keep the registration statement effective until the shares are eligible to be sold under Rule 144(k) under the Securities Act or such earlier date as of which all of the shares have been sold. See the discussion below under **Registration Rights** for more information regarding the selling stockholders' rights under the purchase agreement.

In December 2006, we issued UMMS 150,000 shares of our common stock as payment under a license agreement with UMMS. In connection with the issuance of the shares, we agreed with UMMS to include the shares in the first registration statement subsequently filed by us with respect to resales of shares by our security holders.

Selling Stockholder Table

The following table sets forth certain information regarding the ownership of our common stock by the selling stockholders as of April 19, 2007. Beneficial ownership is determined in accordance with the rules of the SEC, and generally includes voting or investment power with respect to shares. The percentage ownership reflected in the table is based on 87,341,129 shares of our common stock outstanding as of April 19, 2007, plus in the case of each selling stockholder, the shares issuable upon exercise of any warrants, options or convertible securities held by such selling stockholder (which are indicated by footnote) that are exercisable or convertible within 60 days of April 19, 2007, but not including shares issuable upon exercise or conversion of any other options, warrants or other securities. Except as otherwise indicated, to our knowledge, each selling stockholder has sole voting and investment power with respect to the shares shown. For purposes of the following table, we have assumed that the selling stockholders will sell all the shares being offered pursuant to this prospectus. An asterisk denotes beneficial ownership of less than 1%.

The selling stockholders named below have advised us that they currently intend to sell the shares set forth below pursuant to this prospectus. Before a stockholder not named below may use this prospectus in connection with an offering of shares, this prospectus must be amended or supplemented to include the name and number of shares beneficially owned by the selling stockholder and the number of shares to be offered. Any amended or supplemented prospectus also will disclose whether any selling stockholder named in that amended or supplemented prospectus has held any position, office or other material relationship with us or any

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of our predecessors or affiliates during the three years prior to the date of the amended or supplemented prospectus.

Security Holders	Shares Beneficially Owned Prior to Offering		Number of Shares Being Offered	Shares Beneficially Owned After Offering	
	Number	Percent		Number	Percent
Capital Ventures International(1)	465,000	*	465,000	0	0
Enable Growth Partners LP(2)	891,419	1.0	595,000	296,419	*
Enable Opportunity Partners LP(3)	117,619	*	70,000	47,819	*
Fidelity Central Investment Portfolios LLC:					
Fidelity Healthcare Central Fund (4)	240,100	*	51,600	188,500	*
Fidelity Destiny Portfolios:					
Destiny I (4)	693,500	*	193,500	500,000	*
Fidelity Mt. Vernon Street Trust:					
Fidelity Aggressive Growth Fund (4)	6,177,802	*	228,330	5,949,472	6.8
Fidelity Mt. Vernon Street Trust:					
Fidelity New Millennium Fund (4)	3,063,304	*	140,610	2,922,694	3.4
Fidelity Securities Fund:					
Fidelity Advisor Aggressive Growth Fund (4)	74,718	*	2,580	72,138	*
Fidelity Securities Fund:					
Fidelity OTC Portfolio (4)	1,424,467	*	540,510	883,957	1.0
Fidelity Select Portfolios:					
Healthcare Portfolio (4)	626,180	*	131,580	494,600	*
Variable Insurance Products Fund III:					
Aggressive Growth Portfolio (4)	37,454	*	1,290	36,164	*
Fort Mason Master, LP(5)	873,363	1.0	873,363	0	0
Fort Mason Partners, LP(5)	56,637	*	56,637	0	0
Franklin Biotechnology Discovery Fund(6)	443,000	*	443,000	0	0

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Franklin Global Healthcare Fund(6)	82,000	*	82,000	0	0
Highbridge International LLC(7)	4,099,623	4.6	230,000	3,869,623	4.4
Hudson Bay Fund LP (8)	332,200	*	332,200	0	0
Hudson Bay Overseas Fund Ltd(9)	422,800	*	422,800	0	0
Iroquois Master Fund Ltd (10)	786,509	*	350,000	436,509	*
LB I Group, Inc. (11)	1,160,000	1.3	1,160,000	0	0
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Security Holders	Shares Beneficially Owned Prior to Offering		Number of Shares Being Offered	Shares Beneficially Owned After Offering	
	Number	Percent		Number	Percent
Pierce Diversified Strategy Master Fund LLC, Ena(12)	35,000	*	35,000	0	0
Portside Growth and Opportunity Fund(13)	1,087,025	1.2	230,000	857,025	*
RA Capital Biotech Fund, LP(14)	569,792	*	569,792	0	0
RA Capital Biotech Fund II, LP(14)	10,208	*	10,208	0	0
Radcliffe SPC, Ltd. for and on behalf of the Class A Segregated Portfolio (15)	465,000	*	465,000	0	0
Truk International Fund, LP(16)	68,088	*	37,600	30,488	*
Truk Opportunity Fund, LLC(17)	675,043	*	197,400	477,643	*
UBS O Connor LLC F/B/O O Connor PIPES Corporate Strategies Master Limited (18)	700,000	*	700,000	0	0
University of Massachusetts	150,000	*	150,000	0	0

(1) Heights Capital Management, Inc., the authorized agent of Capital Ventures International (CVI), has discretionary authority to vote and dispose of the shares held by CVI and may be deemed to be the beneficial owner of these shares. Martin Kobinger, in his capacity as

Investment
Manager of
Heights Capital
Management,
Inc., may also
be deemed to
have investment
discretion and
voting power
over the shares
held by CVI.
Mr. Kobinger
disclaims any
such beneficial
ownership of
the shares. CVI
is affiliated with
one or more
registered
broker-dealers.
CVI purchased
the shares being
registered
hereunder in the
ordinary course
of business and
at the time of
purchase, had
no agreements
or
understandings,
directly or
indirectly, with
any other person
to distribute
such shares.

- (2) Includes
296,419 shares
issuable upon
exercise of
warrants
acquired in prior
private
placements.
Mitch Levine,
Managing
Partner, has
voting and
investment
control over

these securities.
Mr. Levine
disclaims
beneficial
ownership of
these securities.

- (3) Includes 47,619
shares issuable
upon exercise of
warrants
acquired in prior
private
placements.
Mitch Levine,
Managing
Partner, has
voting and
investment
control over
these securities.
Mr. Levine
disclaims
beneficial
ownership of
these securities.

- (4) The entity is a
registered
investment fund
(the Fund)
advised by
Fidelity
Management &
Research
Company (FMR
Co.), a
registered
investment
adviser under
the Investment
Advisers Act of
1940, as
amended. FMR
Co., 82
Devonshire
Street, Boston,
MA 02199, a
wholly owned
subsidiary of
FMR Corp. and

an investment adviser under Section 203 of the Investment Advisers Act of 1940, is the beneficial owner of 12,800,625 shares of common stock of the Company (including shares offered by the prospectus), or 14.7% of the common stock outstanding, as a result of acting as investment adviser to various investment companies registered under Section 8 of the Investment Company Act of 1940, including the selling stockholders to whom this note relates. The holdings are as of April 18, 2007. None of the selling stockholders to whom this note relates has, or within the past three years has had, any position, office or other material relationship with the Company or any of its predecessors or affiliates.

Because such
selling
stockholders
may offer all or
some portion of
the above
referenced
shares pursuant
to this
prospectus or
otherwise, no
estimate can be
given as to the
amount or
percentage of
such securities
that will be held
by

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such selling stockholders upon termination of any such sale. In addition, the selling stockholders to whom this note relates may have sold, transferred or otherwise disposed of all or a portion of such shares since April 18, 2007 in transactions exempt from the registration requirements of the Securities Act of 1933. Such selling stockholders may sell all, part or none of the securities listed above.

- (5) Fort Mason Capital, LLC serves as the general partner of each of Fort Mason Master, L.P. and Fort Mason Partners, L.P. (collectively, the Fort Mason Funds), and, in such capacity, exercises sole voting and investment authority with respect to such

shares.
Mr. Daniel German serves as the sole managing member of Fort Mason Capital, LLC. Fort Mason Capital, LLC and Mr. German each disclaim beneficial ownership of such shares, except to the extent of its or his pecuniary interest therein, if any.

- (6) The selling stockholder is an investment company managed by Franklin Advisers, Inc. An affiliate of Franklin Advisers, Inc. is a registered broker-dealer and a NASD member, which affiliate will not participate in nor receive any compensation in connection with any sale of these shares. Evan McCulloch and Matthew Willey are Portfolio Managers of Franklin Advisers, Inc., and, in such capacity, exercise sole

voting and investment authority with respect to such shares.

- (7) Includes 1,568,041 shares of common stock issuable upon exercise of warrants acquired by Smithfield Fiduciary LLC, a wholly owned subsidiary Highbridge International LLC, in prior private placements. Highbridge Capital Management, LLC is the trading manager of Highbridge International LLC and has voting control and investment discretion over the securities held by Highbridge International LLC. Glenn Dubin and Henry Swieca control Highbridge Capital Management, LLC and have voting control and investment discretion over the securities held by

Highbridge
International
LLC. Each of
Highbridge
Capital
Management,
LLC, Glenn
Dubin and
Henry Swieca
disclaims
beneficial
ownership of
the securities
held by
Highbridge
International
LLC.

- (8) The selling stockholder is affiliated with XTF Capital, LLC and XTF Marketing LLC, both of which are NASD members and neither of which will participate in or receive any compensation in connection with any sale of these shares. Sander Gerber, Yoav Roth and John Doscas share voting and investment power over these securities. Sander Gerber, Yoav Roth and John Doscas disclaim beneficial ownership of the securities held by Hudson Bay Fund, LP.

- (9) The selling stockholder is affiliated with XTF Capital, LLC and XTF Marketing LLC, both of which are NASD members and neither of which will participate in or receive any compensation in connection with any sale of these shares. Sander Gerber, Yoav Roth and John Doscas share voting and investment power over these securities. Sander Gerber, Yoav Roth and John Doscas disclaim beneficial ownership of the securities held by Hudson Bay Overseas Fund, Ltd.
- (10) Include 436,509 shares of common stock issuable upon exercise of warrants acquired in prior private placements. Joshua Silverman has voting and investment control over these securities. Mr. Silverman disclaims

beneficial
ownership of
these securities.

- (11) LB I Group Inc.
is a subsidiary
of Lehman
Brothers
Holdings Inc.
LB I Group Inc.
makes
proprietary
investments.
Lehman
Brothers
Holdings Inc.
and LB I Group
Inc. are
affiliates of
Lehman
Brothers Inc., a
registered
broker-dealer.
Lehman
Brothers Inc.
served as
placement agent
for the securities
that were sold
by the Company
in a private
placement
completed on
April 19, 2007.
Lehman
Brothers Inc.
and its affiliate,
LB I Group Inc.,
are statutory
underwriters in
respect of these
shares. LB I
Group Inc.
acquired these
shares from
Lehman
Brothers Inc. in
the ordinary
course of
business as a
proprietary

investment and without a view to a distribution. LB I Group Inc. has no agreement or understanding, direct or indirect, with any person to sell these shares. From time to time, Lehman Brothers Inc., the affiliated broker-dealer, provides banking services to the Company.

(12) Mitch Levine, Managing Partner, has voting and investment control over these securities. Mr. Levine disclaims beneficial ownership of these securities.

(13) The investment advisor to Portside Growth and Opportunity Fund is Ramius Capital Group, LLC. An affiliate of Ramius Capital Group, LLC is a NASD member, which affiliate will not participate in nor

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receive any compensation in connection with any sale of these shares. Jeffrey C. Smith has sole voting and investment control over these shares. Mr. Smith disclaims beneficial ownership of these securities.

(14) Peter Kolchinsky and Richard Aldrich are the Managers of RA Capital Management, LLC, which serves as the General Partner of each of RA Capital Biotech Fund, L.P. and RA Capital Biotech Fund II, L.P. Each of Mr. Kolchinsky and Mr. Aldrich, by virtue of his role as Manager of the General Partner, has voting and investment authority with respect to such shares.

(15) Pursuant to an investment management agreement, RG Capital Management, L.P. (RG Capital) serves as the investment manager of Radcliffe SPC, Ltd. s Class A Segregated Portfolio. RGC

Management Company, LLC (Management) is the general partner of RG Capital. Steve Katznelson and Gerald Stahlecker serve as the managing members of Management. Each of RG Capital, Management and Messrs. Katznelson and Stahlecker disclaims beneficial ownership of the securities owned by Radcliffe SPC, Ltd. for and on behalf of the Class A Segregated Portfolio.

- (16) Includes 30,488 shares issuable upon exercise of warrants acquired in prior private placements. Michael E. Fein and Stephen E. Saltzstein, as principals of Atoll Asset Management, LLC, the Managing Member of Truk International Fund, LP, exercise investment and voting control over the securities owned by Truk International Fund, LP. Both Mr. Fein and Mr. Saltzstein disclaim beneficial ownership of the securities owned by Truk International Fund, LP.

- (17) Includes 477,643 shares issuable upon exercise of warrants acquired in prior private placements. Michael E. Fein and Stephen E. Saltzstein, as principals of Atoll Asset Management, LLC, the Managing Member of Truk Opportunity Fund, LLC, exercise investment and voting control over the securities owned by Truk Opportunity Fund, LLC. Both Mr. Fein and Mr. Saltzstein disclaim beneficial ownership of the securities owned by Truk Opportunity Fund, LLC.
- (18) Jeff Putman is the Portfolio Manager of UBS O Connor LLC fbo O Connor PIPES Corporate Strategies Master Limited and as such controls the voting and investment power of these shares and thus may be deemed to beneficially own the shares held by UBS O Connor LLC fbo O Connor PIPES Corporate Strategies Master Limited. Mr. Putman disclaims beneficial ownership of the

shares held by UBS
O Connor LLC fbo
O Connor PIPES
Corporate
Strategies Master
Limited.

Relationships with Selling Stockholders

The selling stockholders are institutional investors who acquired the shares of our common stock being offered in a private placement that we completed on April 19, 2007. Some of these institutional investors are affiliated with registered broker-dealers, but these investors acquired the shares covered by this prospectus in the ordinary course of business and have represented to us that, at the time they acquired their shares, they had no agreement or understanding with any person, whether directly or indirectly, to distribute these shares.

Lehman Brothers Inc., which is affiliated with LBI Group Inc., one of the selling stockholders, acted as lead placement agent in connection with our offer and sale of the shares to the selling stockholders. We paid Lehman Brothers Inc. a cash placement fee at the closing equal to 7% of the gross proceeds from the sale of the shares. We also have reimbursed Lehman Brothers Inc. for its legal expenses. Lehman Brothers Inc. paid a portion of its placement fee to three other broker-dealers who acted as co-placement agents in connection with the sale of the shares.

UMMS has been our principal collaborator with respect to our RNAi technology, and we have entered into several license and other agreements with UMMS as described under the caption **About RXi Material Licenses and Other Agreements** in this prospectus.

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

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Registration Rights

In connection with our sale of the shares to the selling stockholders, we entered into a purchase agreement with the selling stockholders under which we agreed that we would, at our cost:

Within 15 days following the closing date of our sale of the shares, file a registration statement under the Securities Act covering resales of the shares;

Use our best efforts to cause the registration statement to become effective under the Securities Act within the earlier of five days after the SEC has advised us that the registration statement will not be reviewed or 60 days after the closing date or, if the registration statement is selected for review by the SEC, 90 days after the closing date;

Promptly prepare and file with the SEC such amendments and supplements to the registration statement and this prospectus as may be necessary to keep the registration statement effective until the earliest of (i) two years after the effective date of the registration statement, (ii) such time as all of the shares have been sold pursuant to the registration statement, and (iii) such time as the shares become eligible for resale by non-affiliates pursuant to Rule 144(k) under the Securities Act or any other rule of similar effect; and

For a period of two years from the closing, use our commercially reasonable efforts to comply with the requirements of Rule 144 under the Securities Act, including our commercially reasonable efforts to comply with the requirements of Rule 144(c) with respect to public information about us and to timely file all reports required to be filed by us under the Exchange Act.

It may become necessary to suspend the effectiveness of the registration statement or the use of this prospectus in some circumstances, including circumstances relating to pending corporate developments. If the selling stockholders are prohibited from selling shares under the registration statement as a result of a suspension of more than 30 days or suspensions on more than two occasions of not more than 30 days each in any 12-month period, then for each day a suspension is in effect that exceeds the maximum allowed period for a suspension or suspensions, but not including any day on which a suspension is lifted, we will be required to pay the selling stockholders, as liquidated damages, an amount per 30-day period equal to 1.0% of the purchase price paid by the selling stockholder for such of the shares as are owned by the selling stockholder at such time for each day up to a maximum aggregate liquidated damages of 16% of the purchase price of such shares (approximately \$5.9 million).

The following requirements and restrictions will generally apply to a stockholder selling shares pursuant to the registration statement:

The stockholder will be required to be named as a selling security holder in the related prospectus;

The stockholder will be required to deliver a prospectus to purchasers;

The stockholder will be subject to some of the civil liability provisions under the Securities Act in connection with any sales; and

The stockholder will be bound by the provisions of the purchase agreement, which are applicable to the stockholder (including indemnification obligations).

This summary of the registration rights provisions of the purchase agreement is not complete. This summary is subject to, and is qualified in its entirety by reference to, all the provisions of the purchase agreement. See [Incorporation of Certain Documents by Reference](#) for information on obtaining a copy of the purchase agreement.

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In connection with our issuance of shares to UMMS in December 2006, we agreed with UMMS to include the shares in the first registration statement subsequently filed by us with respect to resales of shares by our security holders.

PLAN OF DISTRIBUTION

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

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

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

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

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

Privately negotiated transactions.

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

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

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

Any combination of any of the foregoing methods of sale.

Any other method permitted pursuant to applicable law.

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

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

In connection with the sale of the shares, the selling stockholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of our common stock in the course of hedging the positions they assume. The selling stockholders may also sell shares short after the effective date of the registration statement of which this prospectus is a part and may deliver the shares described in this prospectus to close out their short positions, or loan or pledge the common stock to

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broker-dealers that in turn may sell these shares. The selling stockholders may also enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares described in this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

The selling stockholders and any broker-dealers or agents that are involved in selling the shares may be deemed to be underwriters within the meaning of the Securities Act in connection with such sales. In such event, any commissions received by such broker-dealers or agents and any profit on the resale of the shares purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. Each selling stockholder has informed us that it does not have any written or oral agreement or understanding, directly or indirectly, with any person to distribute the shares being offered by means of this prospectus.

We are required to pay the fees and expenses of the registration of the shares being offered by the selling stockholders. We also have agreed to indemnify the selling stockholders against certain losses, claims, damages and liabilities, including liabilities under the Securities Act.

Because the selling stockholders may be deemed to be underwriters within the meaning of the Securities Act, they will be subject to the prospectus delivery requirements of the Securities Act, including Rule 172 thereunder. There is no underwriter or coordinating broker acting in connection with the proposed sale of the shares by the selling stockholders.

We agreed with the selling stockholders to keep this prospectus effective until the earliest of (i) two years after the effective date of the registration statement of which this prospectus is a part, (ii) such time as all of the shares have been sold pursuant to the registration statement, and (iii) such time as the shares become eligible for resale by non-affiliates pursuant to Rule 144(k) under the Securities Act or any other rule of similar effect.

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

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

DESCRIPTION OF CAPITAL STOCK

The following is only a summary of the material terms of our common stock, preferred stock and stock options and warrants. As a summary, it does not contain all the information that may be important to you. You should carefully read the more detailed provisions of our corrected restated certificate of incorporation filed with the Delaware Secretary of State on November 5, 1997, as amended since that time, and our restated bylaws, each of which has been filed with the SEC, as well as applicable provisions of Delaware law.

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Authorized Capitalization

We are authorized to issue up to 125,000,000 shares of common stock, \$0.001 par value per share, and 5,000,000 shares of preferred stock, \$0.01 par value per share, of which 5,000 shares have been designated as Series A Junior Participating Preferred Stock. As of April 30, 2007, 87,341,129 shares of common stock were issued and outstanding. We have no preferred stock outstanding. All of our outstanding shares of common stock, including the shares offered by this prospectus, fully paid and non-assessable.

Subject to our bylaws and Delaware law, our board of directors has the power to issue any of our unissued shares as it determines, including the issuance of any shares or class of shares with preferred, deferred or other special rights.

Common Stock

Holders of common stock are entitled to one vote per share on all matters submitted to a vote of our stockholders, including with respect to the election of directors, are entitled to receive dividends in cash or in property on an equal basis, if and when dividends are declared on the common stock by our board of directors, subject to any preference in favor of outstanding shares of preferred stock, if there are any.

In the event of our liquidation, all holders of common stock will participate on an equal basis with each other in our net assets available for distribution after payment of our liabilities and any liquidation preference in favor of outstanding shares of preferred stock, if there are any.

Holders of common stock are not entitled to preemptive rights, and the common stock is not subject to redemption.

The rights of holders of common stock are subject to the rights of holders of any preferred stock that we designate or have designated. The rights of preferred stockholders may adversely affect the rights of the common stockholders.

Preferred Stock

Our board of directors has designated 5,000 shares of our authorized preferred stock as Series A Junior Participating Preferred Stock, which have the rights, preferences and privileges summarized below. There are no outstanding shares of Series A Junior Participating Preferred Stock. We have reserved all of the shares of our Series A Junior Participating Preferred Stock for issuance upon exercise of the rights under our Shareholder Protection Rights Agreement described below.

Holders of Series A Junior Participating Preferred Stock will be entitled to vote on any matter with the holders of common stock. The number of votes per whole share of Series A Junior Participating Preferred Stock will be equivalent to the number of votes to which a holder of 100 shares, as adjusted from time to time, of our common stock would be entitled.

Holders of Series A Junior Participating Preferred Stock will be entitled to receive dividends on each date dividends are paid to the holders of common stock in an amount per whole share of Series A Junior Participating Preferred Stock equivalent to the amount a holder of 100 shares, as adjusted from time to time, of our common stock would receive. Holders of Series A Junior Participating Preferred Stock also will be entitled to receive an additional quarterly dividend in an amount per whole share equal to the excess (if any) of \$1.00 over the aggregate dividends paid per whole share of Series A Junior Participating Preferred Stock during the quarter. Dividends on the Series A Junior Participating Preferred Stock shall be cumulative.

As long as any shares of Series A Junior Participating Preferred Stock are outstanding, no dividend on our common stock (other than a dividend in common stock or other stock ranking junior to Series A Junior

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Participating Preferred Stock) may be paid, unless the full cumulative dividends on all outstanding shares of Series A Junior Participating Preferred Stock have been paid.

In the event of a merger, consolidation, reclassification or other transaction where our common stock is exchanged for other stock, securities, cash or any other property, any outstanding shares of Series A Junior Participating Preferred Stock will similarly be exchanged in an amount per whole share equal to the aggregate amount of stock, securities, cash, or other property a holder of 100 shares, as adjusted from time to time, of common stock would receive.

In the event of our liquidation, before any distribution or payment is made to the holders of common stock or to any other stock ranking junior to the Series A Junior Participating Preferred Stock, a holder of Series A Junior Participating Preferred Stock will be entitled to, per whole share of Series A Junior Participating Preferred Stock, the greater of \$1.00 or the equivalent of the aggregate amount distributed or to be distributed to the holder of 100 shares, as adjusted from time to time, of common stock.

The Series A Junior Participating Preferred Stock is not redeemable.

Shares of Series A Junior Participating Preferred Stock may be issued by our board of directors without the approval of our stockholders. The issuance of Series A Junior Participating Preferred Stock would adversely affect the voting power, liquidation rights and other rights held by owners of common stock.

In addition to Series A Junior Participating Preferred Stock, our board of directors is authorized to issue shares of our authorized preferred stock in one or more other series and to fix the voting rights, liquidation preferences, dividend rights, conversion rights, redemption rights and terms, including sinking provisions, and other rights and preferences. Our board of directors determination to issue preferred stock could make it more difficult for a third party to acquire control of our company, or could discourage any such attempt. We have no present plan or intention to issue any preferred stock.

Shareholder Rights Protection Agreement

On April 16, 1997, our board of directors declared a distribution of one right for each outstanding share of our common stock, payable to shareholders of record at the close of business on May 15, 1997 and with respect to each share of common stock (including treasury shares) issued by us thereafter and prior to the separation time. Each right entitles the registered holder to purchase from us one ten-thousandth (1/10,000th) of a share of our Series A Junior Participating Preferred Stock, at a purchase price of \$30 per share, subject to adjustment. The description and terms of the rights are set forth in a Shareholder Protection Rights Agreement, or Rights Agreement, between us and American Stock Transfer & Trust Co., as Rights Agent, dated April 16, 1997, as amended. The Rights Agreement will expire on April 16, 2017, unless renewed or extended by our board of directors.

The separation time will occur on earlier of (i) ten business days (unless otherwise accelerated or delayed by our board) following public announcement that a person or group of affiliated or associated persons, referred to as an acquiring person, has acquired, obtained the right to acquire, or otherwise obtained beneficial ownership of 15% or more of the then outstanding shares of our common stock, or (ii) ten business days (unless otherwise delayed by our board) following the commencement of a tender offer or exchange offer that would result in the person or group beneficially owning 15% or more of our then outstanding shares of common stock.

Until the separation time, the rights will be evidenced by certificates representing outstanding shares of our common stock, and transfer of any certificates representing outstanding common stock will also constitute the transfer of the rights associated with the common stock represented by such certificate.

The rights are not exercisable until the separation time, and will expire at the close of business on the tenth anniversary of the Rights Agreement, unless earlier terminated by us as described below.

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If the separation time occurs, separate rights certificates will be mailed to holders of record of common stock as of the close of business on the date the separation time occurs. Thereafter, the separate rights certificates alone will represent the rights.

If the flip-in date occurs, that is, the close of business ten business days following our announcement that a person has become an acquiring person, and if we have not terminated the rights as described below, then the rights will entitle the holders to acquire shares of common shares (rather than Series A Junior Participating Preferred Stock) having a value equal to twice the rights exercise price. Instead of issuing shares of common stock upon exercise of the rights following a flip-in-date, we may substitute a combination of cash, property, a reduction in the exercise price of the rights, common stock or other securities (or any combination of the above) with a value equal to the common stock which would otherwise be issuable. In addition, at the option of our board of directors prior to the time that any person becomes the beneficial owner of more than 50% of our outstanding common stock, and rather than payment of the cash purchase price, each right may be exchanged for one share of common stock if a flip-in-date occurs. Notwithstanding any of the foregoing, all rights that are, or (under certain circumstances set forth in the Rights Agreement) were, beneficially owned by any person on or after the date such person becomes an acquiring person will be null and void.

Following the flip-in-date, if we are acquired in a merger or consolidation where we do not survive or our common stock is changed or exchanged, or 50% or more of our assets or assets generating 50% or more of our operating income or cash flow is transferred, in one or more transactions to persons who at that time control us, then each right will entitle the holders to acquire for the exercise price shares of the acquiring party having a value equal to twice the rights exercise price.

The exercise price payable with respect to the rights, and the number of rights outstanding, are subject to adjustment from time to time to prevent dilution in the event of a stock dividend, stock split or reverse stock split, or other recapitalization, which would change the number of shares of our common stock outstanding.

At any time until the close of business on the flip-in-date, our board of directors may terminate the rights without any payment to the holders thereof. Our board of directors may condition termination of the rights upon the occurrence of a specified future time or event.

Until a right is exercised, the holder, as such, will have no rights as a stockholder, including, without limitation, any right to vote or to receive dividends.

Any provisions of the Rights Agreement may be amended at any time prior to the close of business on the flip-in-date without the approval of holders of the rights. Thereafter, the Rights Agreement may be amended without approval of the rights holders in any way, which does not materially adversely affect the interests of the rights holders.

The rights may have certain anti-takeover effects. The rights will cause substantial dilution to a person or group that attempts to acquire us on terms not approved by our board of directors (with, where required by the Rights Agreement, the concurrence of a majority of the continuing directors), unless the offer is conditioned on a substantial number of rights being acquired. However, the rights should not interfere with any merger, statutory share exchange or other business combination approved by a majority of our directors, since the rights may be terminated by our board of directors at any time on or prior to the close of business ten business days after our announcement that a person has become an acquiring person. Thus, the rights are intended to encourage persons who may seek to acquire control of us to initiate such an acquisition through negotiations with our board of directors. The effect of the rights may nonetheless be to discourage a third party from making a partial tender offer for our common stock, or otherwise attempting to obtain a substantial ownership in our common stock, or seeking to obtain control of us. To the extent any potential acquirors are deterred by the rights, the rights may have the effect of preserving incumbent management in office.

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A copy of the Rights Agreement has been filed with the SEC as an exhibit to our Current Report on Form 8-K dated April 16, 1997. The above summary description of the rights does not purport to be complete and is qualified in its entirety by reference to the Rights Agreement.

Options and Warrants

As of April 30, 2007, there were outstanding stock options and warrants to purchase approximately 22.4 million shares of our common stock at weighted-average exercise price of \$1.87 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.

All or substantially all of our outstanding warrants contain antidilution provisions pertaining to dividends or distributions with respect to our common stock that could be triggered upon our intended dividend or distribution of RXi shares. Our outstanding warrants to purchase approximately 1.4 million shares contain antidilution provisions that are triggered upon any issuance of securities by us below the prevailing market price of our common stock. In the event that these 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 the event of our consolidation or merger, a sale of all or substantially all of our assets or a compulsory share exchange, the holders of the warrants will be entitled to receive upon exercise of the warrants the same kind and amount of cash, securities or other property which would be receivable by the holder of a number of shares of our common stock for which the warrants are then exercisable.

Holders of options and warrants do not have any of the rights or privileges of our stockholders, including voting rights, prior to exercise of the options and warrants. We have reserved sufficient shares of authorized common stock to cover the issuance of common stock subject to our outstanding options and warrants.

As of April 30, 2007, we had registered with the SEC for resale by our stockholders a total of 59.9 shares of our outstanding shares of common stock, including the 8,765,000 shares being offered under this prospectus, and an additional 22.4 million shares of our common stock issuable upon exercise of outstanding options and warrants. The availability of these shares for public resale, as well as actual resales of these shares, could adversely affect the trading price of our common stock.

Transfer Agent and Registrar

The transfer agent for our common stock is American Stock Transfer & Trust Co., 40 Wall Street, New York, New York 10005.

Certain Anti-Takeover Provisions

Certain provisions of Delaware law, our certificate of incorporation and our bylaws may make it more difficult to acquire control of us by various means. These provisions could deprive the stockholders of opportunities to realize a premium on the shares of stock owned by them. In addition, they may adversely affect the prevailing market price of the stock.

Table of Contents***Delaware Law***

We are subject to the anti-takeover provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the interest stockholder attained that status with the approval of the board of directors or unless the business combination is approved in a prescribed manner. Business combinations include mergers, asset sales and other transactions resulting in a financial benefit to the interested stockholder. Generally, an interested stockholder is a person who, together with his affiliates and associates, owns, or within the prior three years did own, 15% or more of the corporation's voting stock.

Classified Board of Directors

Our certificate of incorporation provides for a classified board of directors consisting of three classes of directors with staggered three-year terms, with each class consisting, as nearly as possible, of one-third of the total number of directors. As a result, approximately one-third of the board of directors will be elected each year. These provisions are likely to increase the time required for stockholders to change the compositions of our board of directors. For example, in general at least two annual meetings will be necessary for stockholders to effect a change in the majority of our board of directors.

Special Stockholder Meetings

Our bylaws provide that special meetings of the stockholders for any purpose or purposes may be called by our board of directors or our officers as instructed by our board of directors. This limitation on the ability to call a special meeting could make it more difficult for stockholders to initiate actions that are opposed by the board. These actions could include the removal of an incumbent director or the election of a stockholder nominee as a director. They could also include the implementation of a rule requiring stockholder ratification of specific defensive strategies that have been adopted by the board with respect to unsolicited takeover bids. In addition, the limited ability to call a special meeting of stockholders may make it more difficult to change the existing board and management.

Amendment of Bylaws

Our certificate of incorporation authorizes our board of directors to amend and repeal our bylaws without stockholder vote.

Advance Notice Requirements for Stockholders Proposals and Director Nominations

Our bylaws provide that stockholders seeking to bring business before or to nominate candidates for election as directors at an annual meeting of stockholders must provide timely notice of their proposal in writing to the corporate secretary. To be timely, a stockholder's notice must be delivered to or mailed and received at our principal executive office not less than 120 days prior to the first anniversary of the mailing date of the previous year's proxy statement for its annual meeting of stockholders; provided that if no annual meeting of stockholders was held in the previous year or the date of the annual meeting of stockholders has been changed to be more than 30 calendar days earlier than or 60 calendar days after such anniversary, notice by the stockholder, to be timely, must be so received not more than 90 days nor later than the later of (i) 60 days prior to the annual meeting of stockholders or (ii) the close of business on the 10th day following the date on which notice of the date of the meeting is given to stockholders or made public, whichever first occurs. Our bylaws also specify requirements as to the form and content of a stockholder's notice. These provisions may impede stockholders' ability to bring matters before an annual meeting of stockholders or make nominations for directors at an annual meeting of stockholders.

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Indemnification of Directors and Officers

Under Section 145 of the Delaware General Corporation Law, we can indemnify our directors and officers against liabilities they may incur in such capacities, including liabilities under the Securities Act of 1933, or Securities Act. Our certificate of incorporation further provides that we are authorized to indemnify our directors and officers to the fullest extent permitted by law through the bylaws, agreement, vote of stockholders or disinterested directors, or otherwise. Our bylaws provide that we will indemnify our directors and officers to the fullest extent permitted by law and require us to advance litigation expenses upon our receipt of an undertaking by the director or officer to repay such advances if it is ultimately determined that the director or officer is not entitled to indemnification. Our bylaws further provide that rights conferred under such bylaws do not exclude any other right such persons may have or acquire under any bylaw, agreement, vote of stockholders or disinterested directors or otherwise.

We also have directors and officers liability insurance. In addition, we have entered into agreements to indemnify our directors and certain of our officers, in addition to the indemnification provided for in the certificate of incorporation and bylaws. These agreements, among other things, indemnify our directors and certain of our officers for certain expenses (including attorneys fees), judgments, fines and settlement amounts incurred by such person in any action or proceeding, including any action by or in our right, on account of services by that person as our director or officer or as a director or officer of any subsidiary of ours, or as a director or officer of any other company or enterprise that the person provides services to at our request.

Our certificate of incorporation provides that, pursuant to Delaware Law, our directors shall not be liable for monetary damages for breach of the directors fiduciary duty of care to us or our stockholders. This provision in the certificate of incorporation does not eliminate the duty of care, and in appropriate circumstances equitable remedies such as injunctive or other forms of non-monetary relief will remain available under Delaware Law. In addition, each director will continue to be subject to liability for breach of the director s duty of loyalty to us or our stockholders, for acts or omissions not in good faith or involving intentional misconduct or knowing violations of law, for actions leading to improper personal benefit to the director, and for payment of dividends or approval of stock repurchases or redemptions that are unlawful under Delaware Law. The provision also does not affect a director s responsibilities under any other law, such as the federal securities laws or state or federal environmental laws.

LEGAL MATTERS

The validity of the securities offered hereby has been passed upon for us by Troy & Gould Professional Corporation, Los Angeles, California. As of April 30, 2007, Troy & Gould Professional Corporation owned 70,000 shares of our common stock and warrants to purchase 7,072 shares of our common stock.

EXPERTS

The consolidated financial statements and schedule and management s report on the effectiveness of internal control over financial reporting incorporated by reference in the Prospectus constituting a part of this Registration Statement have been audited by BDO Seidman, LLP, an independent registered public accounting firm, to the extent and for the year periods set forth in their reports incorporated herein by reference, and are incorporated herein in reliance upon such reports given upon the authority of said firm as experts in auditing and accounting.