GTX INC /DE/
Form 424B5
October 27, 2010

Table of Contents

Filed Pursuant to Rule 424(b)(5)
Registration No. 333-148321

PROSPECTUS SUPPLEMENT
(To the Prospectus dated January 17, 2008)

14,285,715 Shares of Common Stock

We are offering up to 14,285,715 shares of our common stock.

Our common stock is listed on The NASDAQ Global Market under the symbol GTXI . On October 26, 2010, the last reported sale price of our common stock was $3.19 per share.

Investing in our common stock involves significant risks. See Risk Factors beginning on page S-5 of this prospectus supplement.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus supplement. Any representation to the contrary is a criminal offense.

	Per Share	Total
Public offering price	$ 2.80	$ 40,000,002
Underwriting discounts and commissions	$ 0.14	$ 2,000,000
Proceeds, before expenses, to us	$ 2.66	$ 38,000,002

We estimate the total expenses of this offering, excluding the underwriting discounts and commissions, will be approximately $375,000. The underwriter may also purchase up to an additional 2,142,857 shares of our common stock from us at the public offering price, less underwriting discounts and commissions, to cover over-allotments, if any, within 30 days of the date of this prospectus supplement.

We anticipate that delivery of the shares of our common stock will be made through the facilities of the Depository Trust Company on or about November 1, 2010, subject to customary closing conditions.

Sole Book-Running Manager

Lazard Capital Markets

Prospectus supplement dated October 27, 2010

TABLE OF CONTENTS
Prospectus Supplement

Prospectus

ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of the offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part, the accompanying prospectus dated January 17, 2008, including the documents incorporated by reference, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying prospectus or in any document incorporated by reference that was filed with the Securities and Exchange Commission, or SEC, before the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement. If any statement in one of these documents is inconsistent with a statement in another document having a later date for example, a document incorporated by reference in the accompanying prospectus the statement in the document having the later date modifies or supersedes the earlier statement. You should read this prospectus supplement and the accompanying prospectus, including the information incorporated by reference and any free writing prospectus that we have

authorized for use in connection with this offering, in their entirety before making an investment decision.

You should rely only on the information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus, along with the information contained in any free writing prospectus that we have

Table of Contents

authorized for use in connection with this offering. If the description of the offering varies between this prospectus supplement and the accompanying prospectus, you should rely on the information in this prospectus supplement. We have not authorized anyone to provide you with different or additional information. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and in any free writing prospectus that we have authorized for use in connection with this offering is accurate only as of the respective dates of those documents. Our business, financial condition, results of operations and prospects may have changed since those dates.

Table of Contents

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights certain information about us, this offering and information appearing elsewhere in this prospectus supplement, in the accompanying prospectus and in the documents we incorporate by reference. This summary is not complete and does not contain all of the information that you should consider before making an investment decision. To fully understand this offering and its consequences to you, you should read this entire prospectus supplement and the accompanying prospectus carefully, including the factors described under the headings Risk Factors in this prospectus supplement beginning on page S-5, together with any free writing prospectus we have authorized for use in connection with this offering and the financial statements and other information incorporated by reference in this prospectus supplement and the accompanying prospectus.

About GTx, Inc.

Our Business

We are a biopharmaceutical company dedicated to the discovery, development and commercialization of small molecules that selectively target hormone pathways for the treatment and prevention of cancer, the treatment of side effects of anticancer therapy, cancer supportive care, and other serious medical conditions.

We are developing GTx-758, a selective estrogen receptor, or ER, alpha agonist for the treatment of advanced prostate cancer. As a selective ER alpha agonist, GTx-758 has the potential to achieve medical castration by feedback inhibition of the hypothalamic- pituitary-gonadal axis. Because of the mechanism of action of GTx-758, castration is expected to be achieved without concomitant bone loss or the development of hot flashes. In 2009, we evaluated GTx-758 in healthy male volunteers in two Phase I clinical trials. In a single ascending dose study in 96 subjects, GTx-758 was well tolerated and demonstrated a pharmacokinetic profile compatible with daily oral dosing. In a 14 day multiple ascending dose study in 50 subjects, GTx-758 was well tolerated and demonstrated the ability to reduce testosterone and to increase sex hormone binding globulin, or SHBG. In September 2010, we announced that in a Phase II, open label, pharmacokinetic-pharmacodynamic clinical trial in healthy male volunteers, GTx-758 suppressed serum total testosterone to castrate levels, increased serum SHBG, and markedly reduced serum free testosterone, the form of testosterone which is available to prostate cancer cells for growth. Medical castration (levels of serum total testosterone <50 ng/dL) was achieved in subjects receiving both the 1000 mg and 1500 mg treatment. The percentage of treatment compliant subjects receiving 1500 mg of GTx-758 who achieved medical castration was comparable to rates of castration observed with luteinizing hormone releasing hormone treatment, which, along with surgical bilateral orchiectomy, is current standard of care. GTx-758 was well tolerated and no serious adverse events were reported in the study. In 2011, we are planning to initiate an additional clinical trial evaluating GTx-758 for first line treatment in men with advanced prostate cancer.

Additionally, we are developing selective androgen receptor modulators, or SARMs, a new class of drugs with the potential to treat cancer cachexia (cancer induced muscle loss), chronic sarcopenia, which is the loss of skeletal muscle mass resulting in reduced physical strength and ability to perform activities of daily living, and other musculoskeletal wasting or muscle loss conditions. In March 2010, we reacquired full rights to our SARM program, including ostarine , our lead SARM, following the termination by us and Merck & Co., Inc., or Merck, of our exclusive license and collaboration agreement for SARM compounds and related SARM products. We are currently preparing for an End of Phase II meeting with the U.S. Food and Drug Administration, or FDA, that we anticipate will occur later this year, to gain concurrence from the FDA on the proposed late stage clinical development of ostarine for the treatment of cancer cachexia in non-small cell lung cancer patients. Following the FDA s input, we plan to continue our pursuit of a partnership or collaboration for the development and commercialization of SARMs, which includes ostarine for the treatment of cancer cachexia, and/or to initiate a pivotal clinical trial in 2011.

We are also developing toremifene 80 mg, a selective estrogen receptor modulator, or SERM, for the reduction of fractures and treatment of other estrogen deficiency side effects of androgen deprivation therapy, or ADT, in men with prostate cancer. In September 2006, we licensed to Ipsen Biopharm Limited, or Ipsen, exclusive rights in the European Union, Switzerland, Norway, Iceland, Lichtenstein and the Commonwealth of Independent States, which we collectively refer to as the European Territory, to develop and commercialize toremifene in all indications that we have licensed from Orion Corporation, or Orion, which include all indications in humans except the treatment

S-1

and prevention of breast cancer outside of the United States. In December 2008, we submitted a New Drug Application, or NDA, for toremifene 80 mg to reduce fractures in men with prostate cancer on ADT to the FDA. In October 2009, we received a Complete Response Letter from the FDA regarding our NDA for toremifene 80 mg notifying us that the FDA would not approve our NDA in its present form as a result of certain clinical deficiencies identified in the Complete Response Letter.

In March 2010, we amended our collaboration and license agreement with Ipsen primarily to expand our collaboration for the development and commercialization of toremifene 80 mg to reduce fractures in men with prostate cancer and to potentially fund a second pivotal Phase III clinical trial of toremifene 80 mg. In exchange for Ipsen s commitment, subject to specified conditions, to fund a second Phase III clinical trial of toremifene 80 mg, we granted Ipsen certain additional rights, including an expansion of the territory in which Ipsen has the right to develop and commercialize toremifene beyond the European Territory to include Australia and certain countries in North Africa, the Middle East and Asia (excluding Japan), which we collectively refer to as the Ipsen Territory. In addition, Ipsen received the right to co-promote our toremifene 80 mg product candidate for the ADT indication in the United States or, at Ipsen s election in lieu of co-promotion, the right to receive a double digit royalty on net sales of our toremifene 80 mg product candidate for the ADT indication in the United States, which declines as net sales increase beyond an established base. Additionally, Ipsen was released of the obligation to pay certain potential milestone payments totaling 18.0 million related to the European approval of toremifene 80 mg and pricing approvals and received a reduction in the royalty payable to us on aggregate net sales of our toremifene 80 mg product candidate for the ADT indication. Ipsen also received the right of first negotiation, subject to certain conditions, with respect to development, marketing, sale and distribution in the Ipsen Territory of GTx-758.

In April 2010, we submitted a proposed protocol to the FDA for a second pivotal Phase III clinical trial evaluating toremifene 80 mg to reduce fractures in men with prostate cancer on ADT to address in a single clinical trial the deficiencies identified by the FDA in the Complete Response Letter, which we refer to as the planned TREAT 2 trial. Based on our discussions with the FDA to date, we believe that we have finalized the protocol for the planned TREAT 2 trial. Under our amended agreement with Ipsen, Ipsen agreed to pay us up to 42.0 million in clinical development milestones related to a second pivotal Phase III clinical trial evaluating toremifene 80 mg to reduce fractures in men with prostate cancer on ADT. However, our amended agreement with Ipsen provides that if the projected third-party costs of such second pivotal Phase III clinical trial of toremifene 80 mg (our planned TREAT 2 trial) exceed 42.0 million by a certain amount, then we and Ipsen agreed to discuss whether to initiate such trial or to renegotiate the terms of the collaboration. The projected third-party costs of the planned TREAT 2 trial exceed the threshold in excess of 42.0 million established under our amended agreement with Ipsen, and Ipsen has not agreed to the initiation and funding of the planned TREAT 2 trial. We and Ipsen are in discussions with respect to whether to commence the planned TREAT 2 trial and, if so, the renegotiation of the terms of our collaboration, including in particular each party s respective funding commitments related to the planned TREAT 2 trial. Although we continue to be engaged in discussions intended to resolve the matter, we cannot predict the outcome, including whether we will be able to initiate the planned TREAT 2 trial or, if it is initiated, what our respective funding commitments for the planned TREAT 2 trial would be. If we and Ipsen are able to renegotiate the terms of our collaboration and we and Ipsen agree to initiate the planned TREAT 2 trial as proposed, we expect to initiate the planned TREAT 2 trial in the first quarter of 2011.

In May 2010, we announced that toremifene 20 mg failed to meet the primary efficacy endpoint in a completed Phase III clinical trial evaluating toremifene 20 mg for the prevention of prostate cancer in high risk men with high grade prostatic intraepithelial neoplasia, or high grade PIN. We are reviewing all of the data from the Phase III clinical trial to better understand the trial results and the ability of toremifene 20 mg to reduce cancer among high risk men, but we do not currently expect to conduct additional clinical trials evaluating toremifene 20 mg for the prevention of prostate cancer in high risk men with high grade PIN or to submit a NDA to the FDA for this indication.

We market FARESTON® (toremifene citrate) 60 mg tablets, approved for the treatment of advanced metastatic breast cancer in postmenopausal women in the United States. The active pharmaceutical ingredient in FARESTON® is the same as in our toremifene 80 mg product candidate. In January 2005, we acquired from Orion the right to market

Table of Contents

FARESTON® tablets in the United States for the metastatic breast cancer indication. We also acquired from Orion a license to toremifene for all indications in humans worldwide, except breast cancer outside of the United States.

Recent Financial Results

While we have not finalized our full financial results for the three and nine months ended September 30, 2010, we expect to report that we had $19.7 million of cash, cash equivalents and short-term investments as of September 30, 2010, which does not include the final $5.0 million research and development expense reimbursement payment from Merck that we will receive later this year, and we also expect to report that our total costs and expenses were $9.9 million and $36.1 million for the three and nine months ended September 30, 2010, respectively.

Corporate Information

We were originally incorporated under the name Genotherapeutics, Inc. in Tennessee in September 1997. We changed our name to GTx, Inc. in 2001, and we reincorporated in Delaware in 2003. Our principal executive office is located at 175 Toyota Plaza, Suite 700, Memphis, Tennessee, and our telephone number is (901) 523-9700. Our website address is www.gtxinc.com. The information contained in, or that can be accessed through, our website is not part of, and is not incorporated into, this prospectus supplement or the accompanying prospectus and should not be considered a part of this prospectus supplement or the accompanying prospectus.

Unless the context requires otherwise, references in this prospectus supplement and the accompanying prospectus to GTx, the company, we, us and our refer to GTx, Inc. Service marks, trademarks and trade names included or incorporated by reference in this prospectus supplement or the accompanying prospectus are the property of their respective owners.

Table of Contents

The Offering

Common stock offered by us pursuant to this prospectus supplement	14,285,715 shares
Common stock to be outstanding immediately after the offering	50,706,616 shares
Use of proceeds	We currently intend to use the net proceeds from this offering for clinical development and other research and development activities and for working capital and general corporate purposes. See Use of Proceeds on page S-29.
NASDAQ Global Market symbol	GTXI
Risk Factors	Investing in our common stock involves significant risks. See Risk Factors beginning on page S-5.

J.R. Hyde, III, the chairman of our board of directors and the beneficial owner of approximately 33.2% of our common stock as of June 30, 2010, has agreed to purchase, directly or through his affiliates, 5,467,857 shares of common stock in this offering at the price offered to the public.

The number of shares of common stock to be outstanding immediately after this offering as shown above is based on 36,420,901 shares of common stock outstanding as of June 30, 2010. This number excludes, as of June 30, 2010:

- 4,536,539 shares of our common stock issuable upon the exercise of options outstanding, having a weighted-average exercise price of $10.89 per share;
- 89,367 shares of our common stock credited to individual non-employee director stock accounts under our Directors Deferred Compensation Plan; and
- an aggregate of 8,283,075 shares of our common stock reserved for future issuance under our stock option and equity incentive plans.

Unless otherwise indicated, this prospectus supplement reflects and assumes no exercise by the underwriter of its over-allotment option.

Table of Contents

RISK FACTORS

Our business is subject to various risks, including those described below. You should consider carefully the following risks, together with all of the other information included in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering, before making an investment decision. If any of these risks actually occurs, our business, financial condition, results of operations and future prospects would likely be materially and adversely affected. In these circumstances, the market price of our common stock would likely decline, and you may lose all or part of your investment.

Risks Related to Our Financial Condition and Need for Additional Financing

We have incurred losses since inception, and we anticipate that we will incur continued losses for the foreseeable future.

We have a limited operating history. As of June 30, 2010, we had an accumulated deficit of $336.8 million. We have incurred losses in each year since our inception in 1997, including net losses of $46.3 million and $51.8 million in 2009 and 2008, respectively. Due to the termination of our collaboration with Merck & Co., Inc., or Merck, and the associated recognition in the first quarter of 2010 of $49.9 million in deferred revenue and the final payment to be received from Merck later in 2010 of $5.0 million of cost reimbursement for research and development activities, we expect to report net income for the year ending December 31, 2010. However, while recognition of this revenue is expected to result in net income for 2010, we expect to incur significant operating losses in 2011 and for the foreseeable future. These losses have had and will continue to have an adverse effect on our stockholders equity and working capital.

In October 2009, we received a Complete Response Letter from the U.S. Food and Drug Administration, or FDA, regarding our New Drug Application, or NDA, for toremifene 80 mg to reduce fractures in men with prostate cancer on ADT notifying us that the FDA would not approve our NDA in its present form as a result of certain clinical deficiencies identified in the Complete Response Letter. As a result, FDA approval of toremifene 80 mg, if it occurs, will be substantially delayed. In addition, significant additional clinical development will be required in order to potentially obtain FDA approval of toremifene 80 mg, including a second pivotal Phase III clinical trial of toremifene 80 mg. We recently expanded our collaboration with Ipsen Biopharm Limited, or Ipsen, pursuant to which Ipsen committed, subject to certain conditions, up to 42.0 million to fund a second pivotal Phase III clinical trial of toremifene 80 mg. However, our amended agreement with Ipsen provides that if the projected third-party costs of such second pivotal Phase III clinical trial of toremifene 80 mg exceed 42.0 million by a certain amount, then we and Ipsen agreed to discuss whether to initiate such trial or to renegotiate the terms of the collaboration. We believe that we have finalized the protocol for a second pivotal Phase III clinical trial evaluating toremifene 80 mg to reduce fractures in men with prostate cancer on ADT to address in a single clinical trial the deficiencies identified by the FDA in the Complete Response Letter, which we refer to as the planned TREAT 2 trial. The projected third-party costs of the planned TREAT 2 trial exceed the threshold in excess of 42.0 million established under our agreement with Ipsen, and Ipsen has not agreed to the initiation and funding of the planned TREAT 2 trial. We and Ipsen are in discussions with respect to whether to commence the planned TREAT 2 trial and, if so, the renegotiation of the terms of our collaboration, including in particular each party s respective funding commitments related to the planned TREAT 2 trial. Although we continue to be engaged in discussions intended to resolve the matter, we cannot predict the outcome, including whether we will be able to initiate the planned TREAT 2 trial or, if it is initiated, what our respective funding commitments for the planned TREAT 2 trial would be. If we and Ipsen determine to initiate the planned TREAT 2 trial as proposed, the portion of the costs of such trial that we would be required to fund could be substantial. Each of our other product candidates are in earlier-stage clinical development, and significant additional clinical development and financial resources will be required to obtain necessary regulatory approvals for our other product candidates, including ostarine and GTx-758, and to develop them into commercially viable products. Accordingly, we do not expect to obtain FDA or any other regulatory approvals to market any of our product candidates in the near future, if at all.

Table of Contents

Because of the numerous risks and uncertainties associated with developing and commercializing small molecule drugs, we are unable to predict the extent of any future losses or when we will become profitable, if at all. We have financed our operations and internal growth primarily through public offerings and private placement of our common stock, as well as payments from our current and former collaborators, including Merck and Ipsen. In March 2010, we and Merck agreed to terminate our collaboration and, as a result, we will not receive any milestone payments or royalties for the development or sale of selective androgen receptor modulators, or SARMs, from Merck, although Merck remains obligated to make a final payment to us this year of $5.0 million for the reimbursement of SARM research and development costs. FARESTON® is currently our only commercial product and, until such time that we receive regulatory approval to market any of our product candidates, if ever, we expect that FARESTON® will account for all of our product revenue. For the six months ended June 30, 2010, we recognized $1.4 million in net revenues from the sale of FARESTON®. If we, Ipsen, and/or any potential future collaborators are unable to develop and commercialize any of our product candidates, if development is further delayed or eliminated, or if sales revenue from any product candidate that receives marketing approval is insufficient, we may never become profitable and we will not be successful.

We will need to raise substantial additional funding and may be unable to raise capital when needed, which would force us to further delay, reduce or eliminate our product development programs or commercialization efforts.

We will need to raise substantial additional capital to:

- fund our operations and conduct clinical trials;
- continue our research and development; and
- commercialize our product candidates, if any such product candidates receive regulatory approval for commercial sale.

We estimate that our current cash and cash equivalent balances, short-term investments, interest income, product revenue from the sale of FARESTON®, and the final payment from Merck of $5.0 million of cost reimbursement, together with the anticipated net proceeds from this offering, will be sufficient to meet our projected operating requirements through the first quarter of 2012. We have based this estimate on our current business plan and assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. In addition, we will need to raise substantial additional capital prior to that time to fully finance our currently-planned clinical trials that we anticipate will be ongoing at that time. Our future funding requirements will depend on many factors, including:

- matters related to our collaborative arrangement with Ipsen, including a determination as to whether we and Ipsen determine to conduct the planned TREAT 2 trial and, if so, the costs that we will be required to bear with respect to the trial and any other continued development, which costs are expected to be substantial;
- the scope, rate of progress and cost of our, Ipsen s and/or any potential future collaborators clinical trials and other research and development activities;
- future clinical trial results;
- the terms and timing of any potential future collaborative, licensing and other arrangements that we may establish;
- the cost and timing of regulatory filings and/or approvals to commercialize our product candidates and any related restrictions, limitations, and/or warnings in the label of an approved product candidate;
- potential future licensing fees, milestone payments and royalty payments, including the amount and timing of any milestone payments that we may receive under our collaborative arrangement with Ipsen, particularly with

respect to any development milestone payments for our planned TREAT 2 trial, if the trial is initiated;

the cost and timing of establishing medical education, sales, marketing and distribution capabilities;

Table of Contents

the cost of establishing clinical and commercial supplies of our product candidates and any products that we, Ipsen, and/or any potential future collaborators may develop;

the effect of competing technological and market developments;

the cost of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights, and the cost of defending any other litigation claims; and

the extent to which we acquire or invest in businesses, products and technologies, although we currently have no commitments or agreements relating to any of these types of transactions.

Until we can generate a sufficient amount of product revenue, which we may never do, we expect to finance future cash needs through public or private equity offerings, debt financings or collaboration and licensing arrangements, or a combination of the above, as well as through interest income earned on the investment of our cash balances and short-term investments, and revenues from the sale of FARESTON®. With the exception of payments that we may receive under our collaboration with Ipsen, we do not currently have any commitments for future external funding. In December 2009, we announced a reduction of approximately 26% of our workforce in order to reduce our operating expenses in connection with the receipt of the Complete Response Letter regarding our NDA for toremifene 80 mg and the associated delay in the potential regulatory approval of toremifene 80 mg. If we are unable to raise additional funds when we need them, we may need to further reduce our expenditures, perhaps significantly, to preserve our cash. The cost-cutting measures that we may take in the future may not be sufficient to enable us to meet our cash requirements, and they may negatively affect our business and growth prospects.

To the extent we raise additional funds by issuing equity securities, our stockholders may experience dilution, and debt financing, if available, may involve restrictive covenants. Any debt financing or additional equity that we raise may contain terms that are not favorable to us or our stockholders. To the extent we raise additional funds through collaboration and licensing arrangements, such as our arrangement with Ipsen, it may be necessary to relinquish rights to some of our technologies or product candidates, or grant licenses on terms that are not favorable to us. Our ability to raise additional funds and the terms upon which we are able to raise such funds may be adversely impacted by the uncertainty regarding our ability to gain FDA approval of toremifene 80 mg, the uncertainty regarding our ability to fully finance our currently-planned clinical trials, and/or current economic conditions, including the effects of the disruptions to and continuing volatility in the credit and financial markets in the United States and worldwide. As a result of these and other factors, we cannot be certain that additional funding will be available on acceptable terms, or at all. If adequate funds are not available when we need them, we may be required to further delay, reduce the scope of or eliminate one or more of our research or development programs, including our SARM and toremifene programs, conduct additional workforce or other expense reductions, or obtain funds through collaborations with others that are on unfavorable terms or that require us to relinquish rights to some of our technologies or product candidates that we would otherwise seek to develop on our own.

Risks Related to Development of Product Candidates

We will not be able to commercialize our product candidates if our preclinical studies do not produce successful results or if our or our collaborators clinical trials do not demonstrate safety and efficacy in humans.

Preclinical and clinical testing is expensive, can take many years and has an uncertain outcome. Success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful, and interim results of a clinical trial do not necessarily predict final results. Typically, the failure rate for development candidates is high. Significant delays in clinical testing could materially impact our product development costs. We do not know whether planned clinical trials will begin on time, will need to be restructured or will be completed on schedule, if at all.

In clinical studies, the efficacy and/or safety results from the trial may be insufficient to support the submission or approval of a NDA with the FDA. For example, we received a Complete Response Letter in October 2009 from the FDA regarding our NDA for toremifene 80 mg to reduce fractures in men with prostate cancer on ADT, notifying us that the FDA would not approve our NDA in its present form as a result of certain clinical deficiencies identified in the Complete Response Letter, which deficiencies may only be addressed by conducting an additional pivotal Phase

III clinical trial of toremifene 80 mg. In addition, in May 2010, we announced that toremifene 20 mg

Table of Contents

failed to meet its primary efficacy endpoint in our Phase III clinical trial of toremifene 20 mg for the prevention of prostate cancer in high risk men with high grade prostatic intraepithelial neoplasia, or high grade PIN. As a result, we do not currently expect to conduct any additional clinical development of toremifene 20 mg for the high grade PIN indication or to submit a NDA to the FDA for this indication.

We, Ipsen, or any potential future collaborators may experience numerous unforeseen events during, or as a result of, preclinical testing and the clinical trial process that could delay or prevent our or our collaborators ability to commercialize our product candidates, including:

- regulators or institutional review boards may not authorize us, Ipsen, or any potential future collaborators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- preclinical or clinical trials may produce negative or inconclusive results, which may require us, Ipsen, or any potential future collaborators to conduct additional preclinical or clinical testing or to abandon projects that we expect to be promising;
- registration or enrollment in clinical trials may be slower than we currently anticipate, resulting in significant delays;
- we, Ipsen, or any potential future collaborators may suspend or terminate clinical trials if the participating patients are being exposed to unacceptable health risks;
- regulators or institutional review boards may suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements; and
- our product candidates may not have the desired effects or may include undesirable side effects.

If any of these events were to occur and, as a result, we, Ipsen, or any potential future collaborators have significant delays in or termination of clinical trials, our costs could increase and our ability to generate revenue could be impaired, which would adversely impact our financial results.

If we, Ipsen, or any potential future collaborators observe serious or other adverse events during the time our product candidates are in development or after our products are approved and on the market, we, Ipsen, or any potential future collaborators may be required to perform lengthy additional clinical trials, may be denied regulatory approval of such products, may be forced to change the labeling of such products or may be required to withdraw any such products from the market, any of which would hinder or preclude our ability to generate revenues.

Although the results from our completed Phase III clinical trial for toremifene 80 mg to reduce fractures and treat other estrogen deficiency side effects of ADT in men with prostate cancer showed that the drug was well tolerated and had a generally favorable safety profile, more subjects experienced a venous thromboembolic event, or VTE, such as a deep vein thrombosis, pulmonary embolism or heart attack, in the toremifene 80 mg treatment group, 17 (2.6%) compared to 7 (1.1%) in the placebo group. Even though the majority of VTEs recorded in the clinical trial occurred in men who were at high risk for a VTE (including: age greater than 80 years, history of VTEs, recent surgical procedure or immobilization) and data from the clinical trial showed that the number of men without any of these independent risk factors for VTEs in whom a VTE occurred during the clinical trial was 5 in the toremifene 80 mg treatment group versus 3 in the placebo group, the FDA will consider the overall safety profile from our clinical trials when making its determination whether to grant marketing approval and to require potential warnings in the label, if approval is granted.

We have conducted a number of studies of toremifene in addition to our clinical trials, including a Thorough QT study (toremifene 80 mg and toremifene 20 mg), a bioequivalence study (toremifene 80 mg), a series of drug-drug interaction studies (toremifene 80 mg and toremifene 20 mg), and a semen quality study (toremifene 20 mg) to assess the effect of toremifene. The results of the Thorough QT study of 250 healthy male volunteers, with 5 parallel cohorts receiving 20 mg, 80 mg or 300 mg doses of toremifene, moxifloxacin, or placebo, showed that toremifene prolonged

the QT interval in a dose dependent manner. The mean change in QTcB (a measurement of QT interval corrected by Bazett s formula) from baseline relative to placebo for toremifene 20 mg was 5.79 milliseconds, for toremifene 80 mg, it was 22.43 milliseconds, and for moxifloxacin, it was 8.83 milliseconds. Since we market

Table of Contents

FARESTON® in the United States under a license agreement with Orion Corporation, or Orion, we notified the FDA of the Thorough QT study results and have proposed modifications to the FARESTON® label in the United States. FDA action on the proposed label changes is pending. Separately, Orion recommended label changes to the European Medicines Agency, or EMEA. In January 2009, the EMEA recommended that the FARESTON® label within the European Union reflect that toremifene should not be given to patients at risk of prolonged QT intervals or other certain heart problems. The results of these completed studies were included as a part of the NDA submission to the FDA for our toremifene 80 mg product candidate to reduce fractures in men with prostate cancer on ADT and will be included as part of any future NDA submission for our toremifene 80 mg product candidate we make to the FDA if we and Ipsen determine to conduct the planned TREAT 2 trial and the results of such trial are positive. In addition, the results of these completed studies will be used to update the label for FARESTON®. The study results could lead to the inclusion of restrictions, limitations and/or warnings in the label of FARESTON® or an approved toremifene 80 mg product candidate, which may adversely affect the marketability of the product or limit the patients to whom the product is prescribed.

In addition, in our Phase II clinical trial for ostarine for the treatment of cancer cachexia (cancer induced muscle loss), we observed mild elevations of hepatic enzymes in a few patients, and in our preclinical studies for ostarine , only at the highest doses, we observed expected selective effects on the reproductive and other target organs in the male population consistent with the stimulating and inhibiting effects on the androgen receptor which is located in these organs.

If the incidence of the events described above increases in number or severity, if a regulatory authority believes that these or other events constitute an adverse effect caused by the drug, or if other effects are identified during clinical trials that we, Ipsen, or any potential future collaborators may conduct in the future or after any of our product candidates are approved and marketed:

- we, Ipsen, or any potential future collaborators may be required to conduct additional preclinical or clinical trials, make changes in labeling of any such approved products, reformulate any such products, or implement changes to or obtain new approvals of our contractors manufacturing facilities;
- regulatory authorities may be unwilling to approve our product candidates or may withdraw approval of our products;
- we may experience a significant drop in the sales of the affected products;
- our reputation in the marketplace may suffer; and
- we may become the target of lawsuits, including class action suits.

Any of these events could prevent approval or harm sales of the affected product candidates or products, or could substantially increase the costs and expenses of commercializing and marketing any such products.

Risks Related to Our Dependence on Third Parties

We are dependent upon our collaborative arrangement with Ipsen to further develop and commercialize toremifene in Ipsen s licensed territories. We may also be dependent upon additional collaborative arrangements to complete the development and commercialization of some of our other product candidates. These collaborative arrangements may place the development and commercialization of our product candidates outside our control, may require us to relinquish important rights or may otherwise be on terms unfavorable to us.

In September 2006, we entered into a collaboration agreement with Ipsen for the development and commercialization of toremifene, which collaboration was amended in March 2010 to, among other things, expand Ipsen s licensed territory for the development and commercializing of toremifene product candidates. Pursuant to the collaboration agreement, as recently amended, Ipsen committed up to 42.0 million to fund a second pivotal Phase III clinical trial of toremifene 80 mg in exchange for certain additional rights we granted to Ipsen, including an expansion of its licensed territory, as well as a reduction in or, in some cases, an elimination of Ipsen s potential future milestone and royalty obligations to us under our original agreement with Ipsen. However, our amended agreement with Ipsen

provides that if the projected third-party costs of such second pivotal Phase III clinical trial of

toremifene 80 mg (our planned TREAT 2 trial) exceed 42.0 million by a certain amount, then we and Ipsen agreed to discuss whether to initiate such trial or to renegotiate the terms of the collaboration. If we do not to initiate the trial, Ipsen would not be obligated to provide any additional funding for the development of toremifene 80 mg. The projected third-party costs of the planned TREAT 2 trial exceed the threshold in excess of 42.0 million established under our agreement with Ipsen, and Ipsen has not agreed to the initiation and funding of the planned TREAT 2 trial. We and Ipsen are in discussions with respect to whether to commence the planned TREAT 2 trial and, if so, the renegotiation of the terms of our collaboration, including in particular each party s respective funding commitments related to the planned TREAT 2 trial. Although we continue to be engaged in discussions intended to resolve the matter, we cannot predict the outcome, including whether we will be able to initiate the planned TREAT 2 trial or, if it is initiated, what our respective funding commitments for the planned TREAT 2 trial would be. In the event we are unable to satisfactorily renegotiate the terms of our agreement with Ipsen, we or Ipsen may determine not to initiate the planned TREAT 2 trial, and Ipsen could elect to terminate our collaboration. The loss of Ipsen as a collaborator in the development or commercialization of toremifene, any disputes over the terms of our collaboration with Ipsen, or any other adverse developments in our relationship with Ipsen, including our inability to satisfactorily renegotiate the terms of our collaboration, could materially harm our business and would substantially increase our need for additional capital. For example, if we were to lose Ipsen as a collaborator, we may not be able to obtain sufficient additional funding to complete the development of toremifene 80 mg. In addition, Ipsen is obligated to initiate and conduct appropriate clinical studies as required by the appropriate regulatory authorities in order to obtain marketing approvals of toremifene in its licensed territory. Any failure on the part of Ipsen to initiate these studies could delay the commercialization of toremifene in its licensed territory. In addition, the receipt of the Complete Response Letter from the FDA in October 2009 has delayed Ipsen s plans to seek marketing approval of toremifene 80 mg in its licensed territory. Moreover, if we and Ipsen (or either of us individually) determines that clinical development of toremifene 80 mg should be further delayed or discontinued, our potential future milestone payments and potential future revenues from the commercialization of toremifene 80 mg would be reduced or eliminated. In addition, we do not currently expect to conduct additional clinical development of toremifene 20 mg for the high grade PIN indication, and we therefore do not currently expect to receive any milestone payments or royalty payments from Ipsen associated with our toremifene 20 mg product candidate.

We may not be successful in entering into additional collaborative arrangements with other third parties, including as a result of any collaboration discussions we chose to pursue for ostarine and GTx-758, and even if we do enter into collaborative arrangements with other parties, such arrangements may not be successful. If we fail to enter into additional collaborative arrangements on favorable terms, it could delay or impair our ability to develop and commercialize our other product candidates and could increase our costs of development and commercialization.

Dependence on collaborative arrangements, including our collaborative arrangement with Ipsen for the development and commercialization of toremifene subjects us to a number of risks, including:

- we are not able to control either the amount and timing of resources that Ipsen devotes to toremifene;
- we may not be able to control the amount and timing of resources that our potential future collaborators may devote to our other product candidates;
- Ipsen or any potential future collaborations may experience financial difficulties or changes in business focus;
- we may be required to relinquish important rights such as marketing and distribution rights;
- under certain circumstances, Ipsen may not be required to commercialize toremifene in its licensed territory if Ipsen determines that it is not commercially reasonable for it to do so;
- pricing reimbursement constraints in Europe, which is part of Ipsen s licensed territory, may diminish the prospects of our receiving royalty payments from Ipsen on aggregate net sales of toremifene if approved for commercial sale in some or all of the countries in Europe;

Table of Contents

should a collaborator fail to develop or commercialize one of our compounds or product candidates, we may not receive any future milestone payments and will not receive any royalties for the compound or product candidate;

business combinations or significant changes in a collaborator s business strategy may also adversely affect a collaborator s willingness or ability to complete its obligations under any arrangement;

under certain circumstances, a collaborator could move forward with a competing product candidate developed either independently or in collaboration with others, including our competitors; and

collaborative arrangements are often terminated or allowed to expire, such as our former collaboration with Merck, which would delay the development and may increase the cost of developing our product candidates.

We may not realize the anticipated benefits from our collaborative arrangement with Ipsen, and may not receive the anticipated benefits from any future collaboration arrangements that we might establish.

We may never receive any of the clinical development milestone payments for our planned TREAT 2 trial provided for under our collaboration agreement with Ipsen if our negotiations with Ipsen are not successful and we determine not to initiate the planned TREAT 2 trial or Ipsen otherwise determines to terminate our collaboration. In addition, we do not currently expect to conduct additional clinical development of toremifene 20 mg for the high grade PIN indication, and we therefore do not currently expect to receive any milestone payments or royalty payments from Ipsen associated with our toremifene 20 mg product candidate. Even if required regulatory approvals to market toremifene are obtained, it is possible that Ipsen will not successfully market and sell any toremifene products in which case we would not receive royalties to the extent that we currently anticipate. Furthermore, our royalty rates under our collaboration and license agreement with Ipsen are subject to a possible reduction if a generic version of toremifene achieves specified sales levels in a major country within its licensed territory. Ipsen also may be entitled to offset a portion of any royalties due to us if Ipsen licenses patent rights from a third party that would otherwise be infringed by Ipsen s use, manufacture, sale or import of toremifene compounds. Moreover, we have agreed to grant Ipsen co-promotion rights in the United States with respect to toremifene 80 mg for the ADT indication, which may, if toremifene 80 mg receives regulatory approval and is commercialized, reduce the amount of product revenue that we would have otherwise received had we commercialized toremifene 80 mg in the United States solely ourselves.

Under our agreement with Ipsen, we and Ipsen have agreed that neither party will seek to commercialize, promote, market or sell certain products within its licensed territory for an agreed period of time subsequent to the time of the first commercial launch of toremifene within its licensed territory. We and Ipsen have also agreed to grant to the other a right of first negotiation with respect to the development, marketing, sale and distribution of any new SERM-based products for the field of the prevention and treatment of prostate cancer or related side effects, or any other indication the parties agree on. We have also agreed to grant to Ipsen a right of first negotiation, subject to certain conditions, with respect to the development, marketing, sale and distribution of GTx-758 in Ipsen s licensed territory. However, there can be no assurance that we will be able to reach an agreement with Ipsen on reasonable terms, or at all, for any new SERM-based products or GTx-758, as applicable.

Ipsen may terminate our collaboration agreement for our uncured breach, upon our bankruptcy, with 12 months prior written notice for any reason and with 30 days prior written notice as a result of legitimate and documented safety concerns, or in the event that either the UTRF license for chemoprevention of prostate cancer or our license and supply agreement with Orion terminates early. If our agreement with Ipsen is terminated, the anticipated future benefits to us from this agreement would be eliminated and the development and commercialization of toremifene, including in Ipsen s licensed territory, would be delayed and could be abandoned. In any such or similar events, we may not realize the anticipated benefits from our collaborative arrangement with Ipsen.

Besides Ipsen, we have in the past established and intend to continue to establish collaborations with third parties to develop and commercialize some of our current and future product candidates, and these collaborations may not be successful or we may otherwise not realize the anticipated benefits from these collaborations. For example, in March 2010, following Merck s determination to discontinue internal development of ostarine , we and Merck mutually

agreed to terminate our collaboration and, as a result, we will not receive any milestone

Table of Contents

payments or royalties for the development or sale of SARMs from Merck. In the future, we may not be able to locate third-party collaborators to develop and market our product candidates, and we may lack the capital and resources necessary to develop our product candidates alone.

If third parties do not manufacture our product candidates in sufficient quantities, in the required timeframe, and at an acceptable cost, clinical development and commercialization of our product candidates would be delayed.

We do not currently own or operate manufacturing facilities, and we rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our product candidates. Our current and anticipated future dependence upon others for the manufacture of our product candidates may adversely affect our future profit margins, if any, and our ability to develop product candidates and commercialize any product candidates on a timely and competitive basis.

We have agreed to purchase from Orion our worldwide requirements of toremifene in a finished tablet form at specified prices under a license and supply agreement. Similarly, Ipsen has agreed to purchase from Orion toremifene tablets for clinical testing and commercial sale in its licensed territory under an amended supply agreement with Orion. As such, both we and Ipsen rely on Orion as the single source supplier of toremifene.

Orion may terminate its supply obligations at its election at any time as a result of our failure to obtain regulatory approval of one of our toremifene product candidates in the United States prior to December 31, 2009, although we have received no indication from Orion to date that it intends to do so. If Orion elects to terminate its obligation to manufacture and supply us and Ipsen with toremifene, any arrangements we make for an alternative supply would have to be made with a qualified alternative supplier with appropriate FDA approval in order for us to obtain our supply requirements for toremifene. In addition, although Orion s composition of matter patents have expired, and as such, neither we nor Ipsen would be prevented from manufacturing toremifene within the United States or European Territory, there is no obligation on the part of Orion to transfer its manufacturing technology to us or Ipsen or to assist us or Ipsen in developing manufacturing capabilities to meet our respective supply needs. We and Ipsen have mutually agreed to cooperate in the manufacture of toremifene in the event that Orion elects to terminate its obligation to manufacture and supply us and Ipsen with toremifene. Although we and Ipsen have agreed to cooperate with each other in the event either of our supply rights are terminated by Orion for any reason, a disruption in the supply of toremifene could delay the development of and impair our and Ipsen s ability to commercialize toremifene. In addition, in the event of such a termination by Orion, Ipsen could elect to exercise its right to terminate our collaboration agreement on limited notice to us.

We also rely on Orion to cooperate with us in the filing and maintenance of regulatory filings with respect to the manufacture of toremifene, and Orion may terminate its obligation to assist us in obtaining and maintaining regulatory approval of toremifene at its election at any time. If Orion terminates its obligation to cooperate in these activities, or does not cooperate with us or otherwise does not successfully file or maintain these regulatory filings, we would be required to make arrangements with a qualified alternative supplier, which could further delay or prevent regulatory approval of toremifene.

Historically, we have relied on third party vendors for the manufacture of ostarine drug substance. However, Merck assumed primary manufacturing responsibilities for ostarine under our exclusive license and collaboration agreement with Merck, which agreement was terminated in March 2010. In connection with the termination of the agreement with Merck, Merck agreed to return to us all remaining inventory of ostarine drug substance. If this supply of ostarine becomes unusable or if the contract manufacturers that we are currently utilizing to meet our supply needs for ostarine or our other SARM product candidates prove incapable or unwilling to continue to meet our supply needs, we could experience a further delay in conducting any additional clinical trials of ostarine or other SARM product candidates. In addition, we rely on third party contractors for the manufacture of GTx-758 drug substance. We may not be able to maintain or renew our existing or any other third-party manufacturing arrangements on acceptable terms, if at all. If we are unable to continue our relationship with Orion for toremifene, or to do so at an acceptable cost, or other suppliers fail to meet our requirements for GTx-758, or ostarine or our other SARM product candidates for any reason, we would be required to obtain alternate suppliers. Any inability to obtain alternate suppliers, including an inability to obtain approval from the FDA of an alternate supplier, would delay or prevent the clinical development and commercialization of these product candidates.

Table of Contents

Use of third-party manufacturers may increase the risk that we will not have adequate supplies of our product candidates.

Reliance on third-party manufacturers entails risks, to which we would not be subject if we manufactured product candidates or products ourselves, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party because of factors beyond our control;
- the possible termination or non-renewal of the agreement by the third party, based on its own business priorities, at a time that is costly or inconvenient for us;
- drug product supplies not meeting the requisite requirements for clinical trial use; and
- the possible exercise by Orion of its right to terminate its obligation to supply us with toremifene, which it may do at its election at any time.

If we are not able to obtain adequate supplies of our product candidates, it will be more difficult for us to develop our product candidates and compete effectively. Our product candidates and any products that we, Ipsen and/or our potential future collaborators may develop may compete with other product candidates and products for access to manufacturing facilities. For example, the active pharmaceutical ingredient in our toremifene 80 mg product candidate is also the active pharmaceutical ingredient in FARESTON®. Further, Orion has agreed to supply toremifene tablets to Ipsen for clinical trials and commercial supply in its licensed territory. Orion also manufactures toremifene for third parties for sale outside the United States for the treatment of metastatic breast cancer in postmenopausal women.

Our present or future manufacturing partners may not be able to comply with FDA-mandated current Good Manufacturing Practice regulations, other FDA regulatory requirements or similar regulatory requirements outside the United States. Failure of our third-party manufacturers or us to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approval of our product candidates, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates.

If third parties on whom we rely do not perform as contractually required or expected, we may not be able to obtain regulatory approval for or successfully commercialize our product candidates.

We do not have the ability to independently conduct clinical trials for our product candidates, and we must rely on third parties, such as contract research organizations, medical institutions, clinical investigators and contract laboratories to conduct our clinical trials. In addition, we rely on third parties to assist with our preclinical development of product candidates. If these third parties do not successfully carry out their contractual duties or regulatory obligations or meet expected deadlines, if the third parties need to be replaced, or if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for other reasons, our preclinical development activities or clinical trials may be extended, delayed, suspended or terminated, and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates.

Risks Related to Our Intellectual Property

If we lose our licenses from the University of Tennessee Research Foundation, or UTRF, we may be unable to continue a substantial part of our business.

We have licensed intellectual property rights and technology from UTRF used in a substantial part of our business. These license agreements may be terminated by UTRF if we are in breach of our obligations under, or fail to perform any terms of, the agreement and fail to cure that breach. If any of these agreements were terminated,

then we may lose our rights to utilize the technology and intellectual property covered by that agreement to market, distribute and sell our licensed products, which may prevent us from continuing a substantial part of our business and may result in a serious adverse effect on our financial condition, results of operations and any prospects for growth. Additionally, the termination of our UTRF license for chemoprevention of prostate cancer could lead to a termination of our license and collaboration agreement with Ipsen, which would result in a loss of any potential milestone or royalty payments from Ipsen.

If some or all of our, or our licensors , patents expire or are invalidated or are found to be unenforceable, or if some or all of our patent applications do not result in issued patents or result in patents with narrow or unenforceable claims, or if we are prevented from asserting that the claims of an issued patent cover a product of a third party, we may be subject to competition from third parties with products in the same class of products as our product candidates or products with the same active pharmaceutical ingredients as our product candidates.

Our commercial success will depend in part on obtaining and maintaining patent and trade secret protection for our product candidates, as well as the methods for treating patients in the product indications using these product candidates. We will be able to protect our product candidates and the methods for treating patients in the product indications using these product candidates from unauthorized use by third parties only to the extent that we or our exclusive licensors own or control such valid and enforceable patents or trade secrets. Additionally, Ipsen s ability to successfully market toremifene within a substantial portion of its licensed territory may depend on having marketing and data exclusivity from the appropriate regulatory authorities.

Our rights to certain patents and patent applications relating to SARM compounds that we have licensed from UTRF are subject to the terms of UTRF s inter-institutional agreements with The Ohio State University, or OSU, and our rights to future related improvements in some instances are subject to UTRF s exercise of exclusive options under its agreements with OSU for such improvements.

Even if our product candidates and the methods for treating patients for prescribed indications using these product candidates are covered by valid and enforceable patents and have claims with sufficient scope, disclosure and support in the specification, the patents will provide protection only for a limited amount of time. For example, the patent that we have licensed from Orion covering the composition of matter of toremifene has expired in the United States and abroad. As a result, we will need to rely primarily on the protection afforded by method of use patents relating to the use of toremifene for the relevant prescribed indications that have been issued or may be issued from our owned or licensed patent applications. Also, within its licensed territories, Ipsen may need to rely primarily on the protection afforded by marketing and data exclusivity for the toremifene products that may be sold within the respective territory. To date, many of our applications for method of use patents filed for toremifene outside of the United States are still pending and have not yielded issued patents. Loss of marketing and data exclusivity for any toremifene products that may be commercialized within the territories licensed to Ipsen could adversely affect Ipsen s ability to successfully commercialize these products.

Our and our licensors ability to obtain patents can be highly uncertain and involve complex and in some cases unsettled legal issues and factual questions. Furthermore, different countries have different procedures for obtaining patents, and patents issued in different countries provide different degrees of protection against the use of a patented invention by others. Therefore, if the issuance to us or our licensors, in a given country, of a patent covering an invention is not followed by the issuance, in other countries, of patents covering the same invention, or if any judicial interpretation of the validity, enforceability, or scope of the claims in, or the written description or enablement in, a patent issued in one country is not similar to the interpretation given to the corresponding patent issued in another country, our ability to protect our intellectual property in those countries may be limited. Changes in either patent laws or in interpretations of patent laws in the United States and other countries may materially diminish the value of our intellectual property or narrow the scope of our patent protection.

Even if patents are issued to us or our licensors regarding our product candidates or methods of using them, those patents can be challenged by our competitors who can argue such patents are invalid or unenforceable, lack sufficient written description or enablement, or that the claims of the issued patents should be limited or narrowly construed. Patents also will not protect our product candidates if competitors devise ways of making or using these product candidates without legally infringing our patents. The Federal Food, Drug, and Cosmetic Act and FDA regulations

and policies create a regulatory environment that encourages companies to challenge branded drug

patents or to create non-infringing versions of a patented product in order to facilitate the approval of abbreviated new drug applications for generic substitutes. These same types of incentives encourage competitors to submit new drug applications that rely on literature and clinical data not prepared for or by the drug sponsor, providing another less burdensome pathway to approval.

We also rely on trade secrets to protect our technology, especially where we do not believe that patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. Our employees, consultants, contractors, outside scientific collaborators and other advisors may unintentionally or willfully disclose our confidential information to competitors, and confidentiality agreements may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. Enforcing a claim that a third party illegally obtained and is using our trade secrets is expensive and time-consuming, and the outcome is unpredictable. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how. Failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

Off-label sale or use of third-party toremifene products could decrease sales of any toremifene product candidates that we continue to develop and that are approved for commercial sale, and could lead to pricing pressure if such products become available at competitive prices and in dosages that are appropriate for the indications for which we and Ipsen may continue to develop toremifene.

In all countries in which we hold or have licensed rights to patents or patent applications related to toremifene, the composition of matter patents we license from Orion have expired. As a result, we will need to rely primarily on the protection afforded by method of use patents. Our method of use patents may not protect toremifene from the risk of off-label sale or use of other toremifene products in place of any toremifene product candidates that we continue to develop and that are approved for commercial sale. Physicians are permitted to prescribe legally available drugs for uses that are not described in the drug s labeling and that differ from those uses tested and approved by the FDA or its equivalent. Such off-label uses are common across medical specialties and are particularly prevalent for cancer treatments. Any off-label sales of other toremifene products may adversely affect our or Ipsen s ability to generate revenue from the sale of any toremifene product candidates that we continue to develop and that are approved for commercial sale.

Even in the event that patents are issued from our pending method of use patent applications, competitors could market and sell toremifene products for uses for which FARESTON® has already been approved. Thus, physicians in such countries would be permitted to prescribe these other toremifene products for indications that are protected by our method of use patents or method of use patents issuing from pending patent applications, even though these other toremifene products would not have been approved for those uses, and in most cases, the physician would not be liable for contributing to the infringement of our patents or potential patents. Moreover, because Orion has licensed and could further license other parties to market, sell and distribute toremifene for breast cancer outside the United States, physicians in such countries could prescribe these products sold pursuant to another Orion license off-label. This further increases the risk of off-label competition developing for toremifene for the indications for which we and Ipsen may continue to develop this product candidate. In addition, if no patents are issued with respect to our pending method of use patent applications related to the use of toremifene in the countries outside of the United States where these applications are currently pending, we would not have as extensive patent coverage to prevent competitors from marketing and selling generic versions of toremifene at doses and in formulations equivalent to our toremifene product candidates for the indications covered by our pending method of use patent applications. Also, regulatory authorities may not recognize marketing and data exclusivity for toremifene in the territory we licensed to Ipsen under our collaboration for the treatment of prostate cancer and estrogen deficiency side effects resulting from ADT. If generic versions of toremifene are able to be sold in countries within the territory we licensed to Ipsen for the indications for which Ipsen could potentially market toremifene, the royalties to be paid to us by Ipsen will be reduced if the total generic sales exceed a certain threshold for a certain period of time.

Our license agreement with Orion excludes the use of toremifene in humans to treat breast cancer outside the United States and may limit our ability to market toremifene for human uses outside the United States.

Our exclusive license and supply agreement from Orion excludes the use of toremifene for the treatment of metastatic breast cancer in postmenopausal women outside the United States. Orion has licensed to other parties the

right to market, sell and distribute toremifene for the treatment of advanced breast cancer outside the United States

Table of Contents

and could license additional parties to market, sell and distribute toremifene for this indication outside the United States.

Under the terms of our license agreement with Orion, Orion may require us and Ipsen to modify our final toremifene development plans for specified major markets outside the United States if those development plans could adversely affect Orion s or Orion s other licensees activities related to FARESTON® for breast cancer outside the United States or toremifene-based animal health products. Although we do not believe that our or Ipsen s development plans adversely affect these activities, any future modifications to our or Ipsen s plans imposed by Orion may limit our and Ipsen s ability to maximize the commercial potential of toremifene.

If we infringe intellectual property rights of third parties, it may increase our costs or prevent us from being able to commercialize our product candidates.

There is a risk that we are infringing the proprietary rights of third parties because numerous United States and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields that are the focus of our drug discovery, development, and manufacture and process synthesis efforts. Others might have been the first to make the inventions covered by each of our or our licensors pending patent applications and issued patents and might have been the first to file patent applications for these inventions. In addition, because patent applications can take many years to issue, there may be currently pending applications, unknown to us or our licensors, which may later result in issued patents that cover the production, manufacture, synthesis, commercialization, formulation or use of our product candidates. In addition, the production, manufacture, synthesis, commercialization, formulation or use of our product candidates may infringe existing patents of which we are not aware. Defending ourselves against third-party claims, including litigation in particular, would be costly and time consuming and would divert management s attention from our business, which could lead to delays in our development or commercialization efforts. If third parties are successful in their claims, we might have to pay substantial damages or take other actions that are adverse to our business.

As a result of intellectual property infringement claims, or to avoid potential claims, we might:

- be prohibited from selling or licensing any product that we, Ipsen and/or any potential future collaborators may develop unless the patent holder licenses the patent to us, which the patent holder is not required to do;
- be required to pay substantial royalties or other amounts, or grant a cross license to our patents to another patent holder; or
- be required to redesign the formulation of a product candidate so that it does not infringe, which may not be possible or could require substantial funds and time.

In addition, under our collaboration and license agreement with Ipsen, Ipsen may be entitled to offset a portion of any royalties due to us in any calendar year on account of product sales to pay for costs incurred by Ipsen to obtain a license to any dominant intellectual property rights that are infringed by the products at issue.

Risks Related to Regulatory Approval of Our Product Candidates

If we, Ipsen, or any potential future collaborators are not able to obtain required regulatory approvals, we or such collaborators will not be able to commercialize our product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates and the activities associated with their development and commercialization are subject to comprehensive regulation by the FDA, other regulatory agencies in the United States and by comparable authorities in other countries. Failure to obtain regulatory approval for a product candidate will prevent us or any collaborator from commercializing the product candidate. We have not received regulatory approval to market any of our product candidates in any jurisdiction, and we do not expect to obtain FDA or any other regulatory approvals to market any of our product candidates in the near future, if at all. In addition, we will not receive any clinical development milestone or royalty payments associated with our toremifene 80 mg product candidate if we and/or Ipsen determine to discontinue the development of toremifene 80 mg or, if such development continues, if Ipsen is

Table of Contents

unable to obtain the necessary regulatory approvals to commercialize toremifene 80 mg within its licensed territory. The process of obtaining regulatory approvals is expensive, often takes many years, if approval is obtained at all, and can vary substantially based upon the type, complexity and novelty of the product candidates involved.

Changes in the regulatory approval policy during the development period, changes in or the enactment of additional regulations or statutes, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. For example, the FDA announced in 2008 that, due to staffing and resource limitations, it has given its managers discretion to miss certain timing goals for completing reviews of NDAs set forth under the Prescription Drug User Fee Act, or PDUFA. Although the FDA has since publicly expressed a recommitment to meeting PDUFA deadlines, it remains unclear whether and to what extent the FDA will adhere to PDUFA deadlines in the future. If the FDA were to miss a PDUFA timing goal for one of our product candidates, the development and commercialization of the product candidate could be delayed. In addition, the Food and Drug Administration Amendments Act of 2007, or the FDA Amendments Act, which was enacted in September 2007, expands the FDA s authority to regulate drugs throughout the product life cycle, including enhanced authority to require post-approval studies and clinical trials. Other proposals have been made to impose additional requirements on drug approvals, further expand post-approval requirements and restrict sales and promotional activities. This new legislation, and the additional proposals if enacted, may make it more difficult or burdensome for us or our potential future collaborators to obtain approval of our product candidates. Even if the FDA approves a product candidate, the approval may impose significant restrictions on the indicated uses, conditions for use, labeling, advertising, promotion, marketing and/or production of such product, and may impose ongoing requirements for post-approval studies, including additional research and development and clinical trials. The approval may also impose risk evaluation mitigation strategies, or REMS, on a product if the FDA believes there is a reason to monitor the safety of the drug in the market place. REMS may include requirements for additional training for health care professionals, safety communication efforts and limits on channels of distribution, among other things. The sponsor would be required to evaluate and monitor the various REMS activities and adjust them if need be. The FDA also may impose various civil or criminal sanctions for failure to comply with regulatory requirements, including withdrawal of product approval.

Furthermore, the approval procedure and the time required to obtain approval varies among countries and can involve additional testing beyond that required by the FDA. Approval by one regulatory authority does not ensure approval by regulatory authorities in other jurisdictions.

The FDA has substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. For example, in October 2009, we received a Complete Response Letter from the FDA regarding our NDA for toremifene 80 mg to reduce fractures in men with prostate cancer on ADT notifying us that the FDA would not approve our NDA in its present form as a result of certain clinical deficiencies identified in the Complete Response Letter. As a result, FDA approval of toremifene 80 mg, if it occurs, will be substantially delayed Additionally, if our planned TREAT 2 trial of toremifene 80 mg to reduce fractures and treat other estrogen deficiency side effects of ADT in men with prostate cancer is conducted, it could result in varying interpretations of the data obtained from the clinical trial which could delay, limit or prevent regulatory approval of the product candidate. Furthermore, even if we submit an application to the FDA for marketing approval of a product candidate, it may not result in marketing approval from the FDA.

We do not expect to receive regulatory approval for the commercial sale of any of our product candidates that are in development, including toremifene 80 mg, in the near future, if at all. Furthermore, it is not anticipated that Ipsen will receive the appropriate regulatory approvals to market toremifene within its licensed territory any sooner than we will achieve regulatory approval in the United States, and it likely will be thereafter. The inability to obtain FDA approval or approval from comparable authorities in other countries for our product candidates would prevent us, Ipsen, or any potential future collaborators from commercializing these product candidates in the United States or other countries. See the section entitled Business Government Regulation of our Annual Report on Form 10-K, filed with the SEC on March 15, 2010, for additional information regarding risks associated with marketing approval, as well as risks related to post-approval requirements.

Table of Contents

Risks Related to Commercialization

The commercial success of any products that we, Ipsen, and/or any potential future collaborators may develop, including any toremifene products, will depend upon the market and the degree of market acceptance among physicians, patients, healthcare payors and the medical community.

Any products that we, Ipsen, and/or any potential future collaborators may develop may not gain market acceptance among physicians, patients, health care payors and the medical community. If these products do not achieve an adequate level of acceptance, we may not generate material product revenues or receive royalties to the extent we currently anticipate, and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

efficacy and safety results in clinical trials;

the prevalence and severity of any side effects;

potential advantages over alternative treatments;

whether the products we commercialize remain a preferred course of treatment;

the ability to offer our product candidates for sale at competitive prices;

relative convenience and ease of administration;

the strength of marketing and distribution support; and

sufficient third-party coverage or reimbursement.

We have conducted a number of studies of toremifene in addition to our clinical trials, including a Thorough QT study (toremifene 80 mg and toremifene 20 mg), a bioequivalence study (toremifene 80 mg), a series of drug-drug interaction studies (toremifene 80 mg and toremifene 20 mg), and a semen quality study (toremifene 20 mg) to assess the effect of toremifene. The results of the Thorough QT study of 250 healthy male volunteers, with 5 parallel cohorts receiving 20 mg, 80 mg or 300 mg doses of toremifene, moxifloxacin, or placebo, showed that toremifene prolonged the QT interval in a dose dependent manner. The mean change in QTcB (a measurement of QT interval corrected by Bazett s formula) from baseline relative to placebo for toremifene 20 mg was 5.79 milliseconds, for toremifene 80 mg, it was 22.43 milliseconds, and for moxifloxacin, it was 8.83 milliseconds. Since we market FARESTON® in the United States under a license agreement with Orion, we notified the FDA of the Thorough QT study results and have proposed modifications to the FARESTON® label in the United States. FDA action on the proposed label changes is pending. Separately, Orion recommended label changes to the EMEA. In January 2009, the EMEA recommended that the FARESTON® label within the European Union reflect that toremifene should not be given to patients at risk of prolonged QT intervals or other certain heart problems. The results of these completed studies were included as a part of the NDA submission to the FDA for our toremifene 80 mg product candidate to reduce fractures in men with prostate cancer on ADT and will be included as part of any future NDA submission we make to the FDA for toremifene 80 mg if we and Ipsen determine to conduct the planned TREAT 2 trial and the results of such trial are positive. In addition, the results of these completed studies will be used to update the label for FARESTON®. The study results could lead to the inclusion of restrictions, limitations and/or warnings in the label of FARESTON® or an approved toremifene 80 mg product candidate, which may adversely affect the marketability of the product or limit the patients to whom the product is prescribed.

Our only marketed product generating revenue is FARESTON®, which is subject to a number of risks. These risks may cause sales of FARESTON® to continue to decline.

FARESTON® is currently our only marketed product. FARESTON® is indicated for the treatment of metastatic breast cancer in postmenopausal women. FARESTON® competes against tamoxifen, fulvestrant, and several aromatase inhibitors, including anastrozole, letrozole, and exemestane, for hormonal treatment of breast cancer. Sales

of pharmaceuticals for breast cancer in the SERM class have declined in recent years as aromatase inhibitors have gained market share and we believe this trend will continue. Further, the branded competitors have greater resources and generic competitors are preferred by insurers. Continued sales of FARESTON® also could be impacted by many other factors. The occurrence of one or more of the following risks may cause sales of FARESTON® to decline more than we currently anticipate:

Table of Contents

the loss of the availability of Orion s website to market FARESTON®, which is an important source of advertising;

the loss of one or more of our three largest wholesale drug distributors, which together accounted for approximately 96% of our product sales of FARESTON® for the six months ended June 30, 2010;

any restrictions, limitations, and/or warnings added to the FARESTON® label as a result of our studies of toremifene, including a Thorough QT study and drug interaction studies, or otherwise;

the continued success of competing products, including aromatase inhibitors;

the loss of coverage or reimbursement for FARESTON® from Medicare and Medicaid, private health insurers or other third-party payors;

exposure to product liability claims related to the commercial sale of FARESTON®, which may exceed our product liability insurance;

the failure of Orion to maintain regulatory filings or comply with applicable FDA requirements with respect to FARESTON®;

the introduction of generic toremifene products that compete with FARESTON® for the treatment of breast cancer; and

the loss of Orion, upon which we rely as a single source, as our supplier of FARESTON®.

If we are unable to expand our sales and marketing capabilities or establish and maintain agreements with third parties to market and sell our product candidates, we may be unable to generate product revenue from such candidates.

We have limited experience as a company in the sales, marketing and distribution of pharmaceutical products, and in any event have only limited company personnel to undertake such activities, and we therefore need to expand our sales and marketing capabilities or establish and maintain agreements with third parties to market and sell our product candidates. We may be unable to build our own sales and marketing capabilities and there are risks involved with entering into arrangements with third parties to perform these services, which could delay the commercialization of any of our product candidates if approved for commercial sale. For example, we would be relying on Ipsen to market and distribute our toremifene product candidates if their development continues and they are approved for commercial sale through Ipsen s established sales and marketing network within its licensed territory. If our collaboration and license agreement with Ipsen is terminated for any reason, our ability to sell any of our toremifene product candidates that may be approved for commercial sale in Ipsen s licensed territory would be adversely affected, and we may be unable to develop or engage an effective sales force to successfully market and sell such toremifene product candidates in Ipsen s licensed territory. Currently, we do not have a partner outside of Ipsen s licensed territory for our toremifene product candidates, and our success in regions other than Ipsen s licensed territory may be dependent on our ability to find suitable partners in other regions of the world. In addition, to the extent that we enter into arrangements with third parties to perform sales, marketing and distribution services, our product revenues are likely to be lower than if we market and sell any products that we develop ourselves.

If we, Ipsen, and/or any potential future collaborators are unable to obtain reimbursement or experience a reduction in reimbursement from third-party payors for products we sell, our revenues and prospects for profitability will suffer.

Sales of products developed by us, Ipsen, and/or any potential future collaborators are dependent on the availability and extent of reimbursement from third-party payors. Changes in the reimbursement policies of these third-party payors that reduce reimbursements for FARESTON® and any other products that we, Ipsen and/or any potential

future collaborators may develop and sell could negatively impact our future operating and financial results.

The Medicare Prescription Drug, Improvement and Modernization Act of 2003 established comprehensive Medicare coverage and reimbursement of prescription drugs under Medicare Part D. The prescription drug program

established by this legislation may have the effect of reducing the prices that we, Ipsen, or any potential future collaborators are able to charge for products we, Ipsen, and/or any potential future collaborators develop and sell through the program. This legislation may also cause third-party payors other than the federal government, including the states under the Medicaid program, to discontinue coverage for products that we, Ipsen, and/or any potential future collaborators may develop or to lower the amount that they pay. State Medicaid programs are increasingly requesting manufacturers to pay supplemental rebates and requiring prior authorization for use of drugs where supplemental rebates are not provided.

In March 2010, the United States Congress enacted the Patient Protection and Affordable Care Act and the Health Care and Education Reconciliation Act. This health care reform legislation will increase the number of individuals who receive health insurance coverage and will close a gap in drug coverage under Medicare Part D as established in 2003. However, the newly-enacted legislation also implements cost containment measures that could adversely affect our revenues. These measures include increased drug rebates under Medicaid starting in 2010 for brand name prescription drugs, such as FARESTON®, and extension of these rebates to Medicaid managed care, which would reduce the amount of net reimbursement received for FARESTON® or any other products that we, Ipsen, and/or any potential future collaborators may develop and sell. Also effective for 2010, the legislation extends 340B discounted pricing on outpatient drugs to children s hospitals, critical access hospitals, and rural health centers, which extension reduces the amount of reimbursement received for drugs purchased by these new 340B-covered entities.

Additional provisions of the health care reform legislation, which become effective in 2011, may negatively affect our revenues and prospects for profitability in the future. Along with other pharmaceutical manufacturers and importers of brand name prescription drugs, we will be assessed a fee based on our proportionate share of sales of brand name prescription drugs to certain government programs, including Medicare and Medicaid. As part of the health care reform legislation s provisions closing a funding gap that currently exists in the Medicare Part D prescription drug program (commonly known as the donut hole), we will also be required to provide a 50% discount on brand name prescription drugs, including FARESTON®, sold to beneficiaries who fall within the donut hole.

In the aftermath of the 2010 health care reform legislation, private health insurers and managed care plans are likely to continue challenging the prices charged for medical products and services, and many of these third-party payors may limit reimbursement for newly-approved health care products. In particular, third-party payors may limit the indications for which they will reimburse patients who use any products that we, Ipsen, and/or any potential future collaborators may develop or sell. These cost-control initiatives could decrease the price we might establish for products that we, Ipsen, or any potential future collaborators may develop or sell, which would result in lower product revenues or royalties payable to us.

Similar cost containment initiatives exist in countries outside of the United States, particularly in the countries of the European Union, where the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take six to twelve months or longer after the receipt of regulatory marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we, Ipsen, or any potential future collaborators may be required to conduct a clinical trial that compares the cost effectiveness of our product candidates or products to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in our, Ipsen s or a potential future collaborators commercialization efforts. Third-party payors are challenging the prices charged for medical products and services, and many third-party payors limit reimbursement for newly-approved health care products. In particular, third-party payors may limit the indications for which they will reimburse patients who use any products that we, Ipsen, and/or any potential future collaborators may develop or sell. Cost-control initiatives could decrease the price we might establish for products that we, Ipsen, or any potential future collaborators may develop or sell, which would result in lower product revenues or royalties payable to us.

Another development that could affect the pricing of drugs would be proposed congressional action regarding drug reimportation into the United States. The Medicare Prescription Drug, Improvement and Modernization Act of 2003 gives discretion to the Secretary of Health and Human Services to allow drug reimportation into the United States under some circumstances from foreign countries, including from countries where the drugs are sold at a lower price than in the United States. Provisions allowing for the direct reimportation of drugs under certain

Table of Contents

circumstances were not included in the 2010 health care reform legislation, but could be revisited in the future. If legislation or regulations were passed allowing the reimportation of drugs, they could decrease the price we, Ipsen, or any potential future collaborators receive for any products that we, Ipsen, and/or any potential future collaborators may develop, negatively affecting our revenues and prospects for profitability.

Health care reform measures could hinder or prevent our product candidates commercial success.

Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting health care reform, as evidenced by the recent enactment in the United States of the Patient Protection and Affordable Care Act and the Health Care and Education Reconciliation Act. It is likely that federal and state legislatures within the United States and foreign governments will continue to consider changes to existing health care legislation. These changes adopted by governments may adversely impact our business by lowering the price of health care products in the United States and elsewhere.

We operate in a highly regulated industry and new laws, regulations or judicial decisions, or new interpretations or existing laws, regulations or decisions, related to health care availability, method of delivery or payment for health care products and services, or sales, marketing and pricing practices could negatively impact our business, operations and financial condition.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of any products that we may develop.

We face an inherent risk of product liability exposure related to our commercial sale of FARESTON® and the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any product that we may develop. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

decreased demand for any product candidates or products;

injury to our reputation;

withdrawal of clinical trial participants;

costs to defend the related litigation;

substantial monetary awards to trial participants or patients;

loss of revenue; and

the inability to commercialize any products for which we obtain or hold marketing approvals.

We have product liability insurance that covers our clinical trials and commercial products up to a $25 million annual aggregate limit. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost and we may not be able to obtain insurance coverage that will be adequate to satisfy any liability that may arise.

If our competitors are better able to develop and market products than any products that we, Ipsen, and/or any potential future collaborators may develop, our commercial opportunity will be reduced or eliminated.

We face competition from commercial pharmaceutical and biotechnology enterprises, as well as from academic institutions, government agencies and private and public research institutions. Our commercial opportunities will be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer side effects or are less expensive than any products that we, Ipsen, and/or any potential future collaborators may develop. Competition could result in reduced sales and pricing pressure on our product candidates, if approved, which in turn would reduce our ability to generate meaningful revenue and have a negative impact on our results of operations. In addition, significant delays in the development of our product candidates could allow our competitors to bring products to market before us and impair any ability to commercialize our product candidates.

Table of Contents

Various products are currently marketed or used off-label for some of the diseases and conditions that we are targeting in our pipeline, and a number of companies are or may be developing new treatments. These product uses, as well as promotional efforts by competitors and/or clinical trial results of competitive products, could significantly diminish any ability to market and sell any products that we, Ipsen, and/or any potential future collaborators may develop.

We are developing GTx-758 for the treatment of advanced prostate cancer. Currently, there are several products approved to reduce testosterone levels in men with advanced prostate cancer that may compete with GTx-758 if approved for commercial sale, including those marketed by Abbott Laboratories (Lupron®), Sanofi-Aventis (Eligard ®), AstraZeneca (Zoladex®), Ferring Pharmaceuticals (Firmagon®), Endo Pharmaceuticals (Vantas®) and Watson Pharmaceuticals (Trelstar®).

With respect to our SARM program, there are other SARM product candidates in development that may compete with our SARM product candidates if approved. Pfizer Inc., Eli Lilly & Co., and Amgen have myostatin inhibitors in development that may compete with ostarine if approved for commercial sale. In addition, Cytokinetics, Inc. is developing a troponin activator with a muscle specific mechanism in a Phase I study. Moreover, there are other categories of drugs in development, including ghrelin receptor agonists and growth hormone secretagogues that may have some muscle activity. Other appetite stimulants such as megestrol acetate and dronabinol are also used off-label for cancer cachexia.

We are also developing toremifene 80 mg for the reduction of fractures and treatment of other estrogen deficiency side effects of ADT. Although there are no products that have been approved by the FDA to reduce fractures or treat estrogen deficiency related side effects of ADT, we are aware of a number of drugs, including drugs marketed by Eli Lilly & Co. (Evista®), Merck (Fosamax®), Sanofi-Aventis and Warner Chilcott (Actonel®), Pfizer Inc. (Effexor®), Boehringer Ingelheim (Catapres®), Novartis (Zometa®) and generic megestrol acetate, that are prescribed to treat single side effects of ADT; that external beam radiation and tamoxifen are used to treat breast pain and enlargement, or gynecomastia. ProliaTM (denosumab), a monoclonal antibody developed by Amgen, is approved in the United States, Europe and Australia for the treatment of osteoporosis in postmenopausal women and additionally in Europe for the treatment of bone loss associated with hormone ablation in men with prostate cancer at increased risk of fractures, and is under regulatory review for cancer specific indications including prostate cancer.

Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies and technology licenses complementary to our programs or advantageous to our business.

Risks Related to Employees and Growth

If we fail to attract and keep senior management and key scientific personnel, we may be unable to successfully develop or commercialize our product candidates.

Our success depends on our continued ability to attract, retain and motivate highly qualified management, clinical and scientific personnel and on our ability to develop and maintain important relationships with leading academic institutions, clinicians and scientists. If we are not able to attract and keep senior management and key scientific personnel, particularly Dr. Mitchell S. Steiner, we may not be able to successfully develop or commercialize our product candidates. All of our employees are at-will employees and can terminate their employment at any time. We do not carry key person insurance covering members of senior management, other than $25 million of insurance covering Dr. Steiner.

In December 2009, we announced a reduction of approximately 26% of our workforce in order to reduce our operating expenses in connection with the receipt of the Complete Response Letter regarding our NDA for

Table of Contents

toremifene 80 mg and the associated delay in the potential regulatory approval of toremifene 80 mg. This and any future workforce reductions may negatively affect our ability to retain or attract talented employees.

We will need to hire additional employees in order to commercialize our product candidates in the future. Any inability to manage future growth could harm our ability to commercialize our product candidates, increase our costs and adversely impact our ability to compete effectively.

In order to commercialize our product candidates in the future, we will need to expand the number of our managerial, operational, financial and other employees and the competition for qualified personnel in the biotechnology field is intense.

Future growth will impose significant added responsibilities on members of management, including the need to identify, recruit, maintain and integrate additional employees. Our future financial performance and our ability to commercialize our product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively.

Risks Related to this Offering and Ownership of our Common Stock

Market volatility may cause our stock price and the value of your investment to decline.

The market prices for securities of biotechnology companies in general have been highly volatile and may continue to be so in the future. The following factors, in addition to other risk factors described in this section, may have a significant impact on the market price of our common stock:

- developments with respect to our collaboration with Ipsen, including the results of our negotiations with Ipsen with respect to the planned TREAT 2 trial, any changes to the terms of our collaboration, and any determination by Ipsen to terminate the collaboration;
- adverse results or delays in our clinical trials;
- our ability to enter into additional collaborative arrangements with respect to our product candidates;
- the timing of achievement of, or failure to achieve, our, Ipsen s and any potential future collaborators clinical, regulatory and other milestones, such as the commencement of clinical development, the completion of a clinical trial or the receipt of regulatory approval;
- announcement of FDA approval or non-approval of our product candidates or delays in the FDA review process;
- actions taken by regulatory agencies with respect to our product candidates or products, our clinical trials or our sales and marketing activities, including regulatory actions requiring or leading to restrictions, limitations and/or warnings in the label of FARESTON® or an approved toremifene product candidate;
- the commercial success of any product approved by the FDA or its foreign counterparts;
- introductions or announcements of technological innovations or new products by us, Ipsen, potential future collaborators, or our competitors, and the timing of these introductions or announcements;
- market conditions for equity investments in general, or the biotechnology or pharmaceutical industries in particular;
- the terms and timing of any future collaborative, licensing or other arrangements that we may establish;
- regulatory developments in the United States and foreign countries;
- changes in the structure or reimbursement policies of health care payment systems;

any intellectual property infringement lawsuit involving us;

actual or anticipated fluctuations in our results of operations;

Table of Contents

changes in financial estimates or recommendations by securities analysts;

sales of large blocks of our common stock;

sales of our common stock by our executive officers, directors and significant stockholders;

changes in accounting principles; and

the loss of any of our key scientific or management personnel.

The stock markets in general, and the markets for biotechnology stocks in particular, have experienced significant volatility that has often been unrelated to the operating performance of particular companies. Recently, the financial markets have faced almost unprecedented turmoil, resulting in a decline in investor confidence and concerns about the proper functioning of the securities markets, which decline in general investor confidence has resulted in depressed stock prices for many companies notwithstanding the lack of a fundamental change in their underlying business models or prospects. These broad market fluctuations may adversely affect the trading price of our common stock.

In the past, class action litigation has often been instituted against companies whose securities have experienced periods of volatility in market price. Any such litigation brought against us could result in substantial costs, which would hurt our financial condition and results of operations and divert management s attention and resources, which could result in delays of our clinical trials or commercialization efforts.

Management will have broad discretion as to the use of the proceeds from this offering, and we may not use the proceeds effectively.

Our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. Our failure to apply these funds effectively could have a material adverse effect on our business, delay the development of our product candidates and cause the price of our common stock to decline.

Our executive officers, directors and largest stockholders have the ability to control all matters submitted to stockholders for approval.

As of June 30, 2010, our executive officers, directors and holders of 5% or more of our outstanding common stock beneficially owned approximately 66.0% of our outstanding common stock, and our executive officers and directors alone beneficially owned approximately 48.9% of our outstanding common stock. As a result, these stockholders, acting together, may or will have the ability to control all matters requiring approval by our stockholders, including the election of directors and the approval of mergers or other business combination transactions. The interests of this group of stockholders may not always coincide with our interests or the interests of other stockholders.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our certificate of incorporation and our bylaws may delay or prevent an acquisition of us or a change in our management. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our Board of Directors. Because our Board of Directors is responsible for appointing the members of our management team, these provisions could in turn affect any attempt by our stockholders to replace current members of our management team. These provisions include:

a classified Board of Directors;

a prohibition on actions by our stockholders by written consent;

Table of Contents

the ability of our Board of Directors to issue preferred stock without stockholder approval, which could be used to institute a poison pill that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our Board of Directors; and

limitations on the removal of directors.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. Finally, these provisions establish advance notice requirements for nominations for election to our Board of Directors or for proposing matters that can be acted upon at stockholder meetings. These provisions would apply even if the offer may be considered beneficial by some stockholders.

If there are substantial sales of our common stock, the market price of our common stock could drop substantially, even if our business is doing well.

For the 12-month period ended June 30, 2010, the average daily trading volume of our common stock on the NASDAQ Global Market was 406,412 shares. As a result, future sales of a substantial number of shares of our common stock in the public market, or the perception that such sales may occur, could adversely affect the then-prevailing market price of our common stock. As of June 30, 2010, we had 36,420,901 shares of common stock outstanding.

We, along with our executive officers and directors, have agreed, subject to certain exceptions, to specified lock-up provisions with regard to future sales of our common stock for a period of 90 days after the offering as described under Underwriting No Sales of Similar Securities. The market price for shares of our common stock may drop significantly if stockholders subject to these lock-up provisions sell a substantial number of shares when the restrictions on resale lapse, or such shares are sold pursuant to specified exceptions, or if the underwriter waives these lock-up provisions and allows these stockholders to sell some or all of their shares. Based on information currently available to us, all of the shares to be outstanding after this offering will be eligible for sale in the public market following expiration of these lock-up provisions, subject in some cases to volume and other limitations under federal securities laws.

Moreover, J.R. Hyde, III, and Oracle Investment Management, Inc., two of our largest stockholders, and their affiliates, have rights, subject to some conditions, to require us to file registration statements covering the approximately 10.8 million shares of common stock they hold in the aggregate which are subject to registration rights or to include these shares in registration statements that we may file for ourselves or other stockholders. If any of these large stockholders were to sell large blocks of shares in a short period of time, the market price of our common stock could drop substantially.

If you purchase shares of common stock in this offering, you will experience immediate dilution in your investment. You will experience further dilution if we issue additional equity securities in future fundraising transactions.

Purchasers of common stock in this offering will pay a price per share in this offering that exceeds the net tangible book value per share of our common stock. After giving effect to the sale of 14,285,715 shares of our common stock in this offering at the public offering price of $2.80 per share, and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, you will experience immediate dilution of $1.59 per share, representing the difference between our as adjusted net tangible book value per share as of June 30, 2010 after giving effect to this offering and the public offering price. See the section entitled Dilution below for a more detailed illustration of the dilution you would incur if you purchase common stock in this offering.

If we issue additional common stock, or securities convertible into or exchangeable or exercisable for common stock, our stockholders, including investors who purchase shares of common stock in this offering, will experience

Table of Contents

additional dilution, and any such issuances may result in downward pressure on the price of our common stock. We also cannot assure you that we will be able to sell shares or other securities in any other offering at a price per share that is equal to or greater than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders.

We have never paid dividends on our capital stock and we do not anticipate paying any cash dividends in the foreseeable future.

We have never declared or paid cash dividends on our capital stock. We do not anticipate paying any cash dividends on our capital stock in the foreseeable future. We currently intend to retain all available funds and any future earnings to fund the development and growth of our business. As a result, capital appreciation, if any, of our common stock will be our stockholders sole source of gain for the foreseeable future.

Table of Contents

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

The statements in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference and in any free writing prospectus that we have authorized for use in connection with this offering contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, which we refer to as the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, which we refer to as the Exchange Act. These statements relate to future events or to our future financial performance and involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. All statements, other than statements of historical facts, are forward-looking statements for purposes of these provisions, including without limitation any statements relating to:

- the anticipated progress of our research, development and clinical programs, including whether any future clinical trials we conduct will achieve similar results to clinical trials that we have successfully concluded;
- the timing, scope and anticipated initiation and completion of any future clinical trials that we may conduct;
- the timing of regulatory submissions and the timing, scope and anticipated outcome of related regulatory actions;
- potential future licensing fees, milestone payments and royalty payments, including any milestone payments or royalty payments that we may receive under our collaborative arrangement with Ipsen;
- our ability to maintain our collaborative arrangement with Ipsen and to establish and maintain potential new collaborative arrangements for the development and commercialization of our product candidates;
- our and our current and potential future collaborators ability to obtain and maintain regulatory approvals of our product candidates and any related restrictions, limitations, and/or warnings in the label of an approved product candidate;
- our and our current and potential future collaborators ability to market, commercialize and achieve market acceptance for our product candidates or products that we may develop;
- our ability to generate additional product candidates for clinical testing;
- our ability to protect our intellectual property and operate our business without infringing upon the intellectual property rights of others; and
- our estimates regarding the sufficiency of our cash resources and our use of the net proceeds from this offering.

In some cases, you can identify forward-looking statements by terms such as anticipates, believes, could, estimate expects, intends, may, plans, potential, predicts, projects, should, will, would and similar expressi identify forward-looking statements. Discussions containing these forward-looking statements may be found, among other places, in the Business and Management s Discussion and Analysis of Financial Condition and Results of Operations sections incorporated by reference from our most recent Annual Report on Form 10-K, as well as any amendments thereto reflected in subsequent filings with the SEC, and in Current Reports on Form 8-K filed with the SEC. Forward-looking statements reflect our current views with respect to future events, are based on assumptions and are subject to risks, uncertainties and other important factors. We discuss many of these risks, uncertainties and other important factors in greater detail under the heading Risk Factors in this prospectus supplement. Given these risks, uncertainties and other important factors, you should not place undue reliance on these forward-looking statements. Also, these forward-looking statements represent our estimates and assumptions only as of the date such forward-looking statements are made. You should carefully read this prospectus supplement and the accompanying

prospectus, together with the information incorporated by reference as well as any free writing prospectus we have authorized for use in connection with this offering, completely and with the understanding that our actual future results may be materially different from what we expect. We hereby qualify all of our forward-looking statements by these cautionary statements.

Table of Contents

Except as required by law, we assume no obligation to update any forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in any forward-looking statements, even if new information becomes available in the future.

Table of Contents

USE OF PROCEEDS

We estimate that the net proceeds from the sale of 14,285,715 shares of common stock that we are offering hereby will be approximately $37.6 million, or approximately $43.3 million if the underwriter exercises in full its over-allotment option to purchase additional shares of common stock, based on the public offering price of $2.80 per share, and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

We currently intend to use the net proceeds from this offering for clinical development and other research and development activities and for working capital and general corporate purposes. As of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses of the proceeds from this offering. Accordingly, we will retain broad discretion over the use of such proceeds. Pending the use of the net proceeds from this offering as described above, we intend to invest the net proceeds in investment-grade, interest-bearing instruments.

Table of Contents

DILUTION

Our net tangible book value as of June 30, 2010 was $23.5 million, or $0.65 per share of common stock. Net tangible book value per share is calculated by subtracting our total liabilities from our total tangible assets, and dividing this amount by the number of shares of common stock outstanding.

After giving effect to the sale of 14,285,715 shares of our common stock in this offering at the public offering price of $2.80 per share, and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of June 30, 2010 would have been approximately $61.2 million, or $1.21 per share. This represents an immediate increase in net tangible book value of $0.56 per share to existing stockholders and immediate dilution in net tangible book value of $1.59 per share to new investors purchasing our common stock in this offering at the public offering price. The following table illustrates this dilution on a per share basis:

Public offering price per share		$ 2.80
Historical net tangible book value per share as of June 30, 2010	$ 0.65	
Increase per share attributable to investors participating in this offering	0.56	
As adjusted net tangible book value per share after this offering		1.21
Dilution per share to investors participating in this offering		$ 1.59

If the underwriter exercises in full its over-allotment option to purchase 2,142,857 additional shares of common stock at the public offering price of $2.80 per share, the as adjusted net tangible book value after this offering would be $1.26 per share, representing an increase in net tangible book value of $0.61 per share to existing stockholders and immediate dilution in net tangible book value of $1.54 per share to new investors purchasing our common stock in this offering at the public offering price.

The above discussion and table are based on 36,420,901 shares of our common stock outstanding on June 30, 2010. This number excludes, as of June 30, 2010:

- 4,536,539 shares of our common stock issuable upon the exercise of options outstanding, having a weighted-average exercise price of $10.89 per share;
- 89,367 shares of our common stock credited to individual non-employee director stock accounts under our Directors Deferred Compensation Plan; and
- an aggregate of 8,283,075 shares of our common stock reserved for future issuance under our stock option and equity incentive plans.

Table of Contents

MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES TO NON-U.S. HOLDERS

The following summary describes the material U.S. federal income and estate tax consequences of the acquisition, ownership and disposition of our common stock acquired in this offering by a Non-U.S. Holder (as defined below). This discussion does not address all aspects of U.S. federal income and estate taxes and does not deal with foreign, state and local consequences that may be relevant to Non-U.S. Holders in light of their particular circumstances. Special rules may apply to certain Non-U.S. Holders that are subject to special treatment under the Internal Revenue Code of 1986, as amended, or the Code, such as financial institutions, insurance companies, tax-exempt organizations, broker-dealers and traders in securities, U.S. expatriates, controlled foreign corporations, passive foreign investment companies, corporations that accumulate earnings to avoid U.S. federal income tax, persons that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or integrated investment, partnerships a other pass-through entities, and investors in such pass-through entities. Such Non-U.S. Holders are urged to consult their own tax advisors to determine the U.S. federal, state, local and other tax consequences that may be relevant to them. Furthermore, the discussion below is based upon the provisions of the Code, and Treasury regulations, rulings and judicial decisions thereunder as of the date hereof, and such authorities may be repealed, revoked or modified, perhaps retroactively, so as to result in U.S. federal income and estate tax consequences different from those discussed below. This discussion assumes that the Non-U.S. Holder holds our common stock as a capital asset.

The following discussion is for general information only and is not tax advice. Persons considering the purchase of our common stock should consult their own tax advisors concerning the U.S. federal income and estate tax consequences in light of their particular situations as well as any consequences arising under the laws of any other taxing jurisdiction, including any state, local or foreign tax consequences.

Except as otherwise described in the discussion of estate tax below, a Non-U.S. Holder is a beneficial holder of our common stock that is not a U.S. Holder or an entity treated as a partnership for U.S. tax purposes. A U.S. Holder means a beneficial holder of our common stock that is for U.S. federal income tax purposes (i) an individual who is a citizen or resident of the United States, (ii) a corporation or other entity treated as a corporation created or organized in or under the laws of the United States or any political subdivision thereof, (iii) an estate the income of which is subject to U.S. federal income taxation regardless of its source or (iv) a trust if it (x) is subject to the primary supervision of a court within the United States and one or more U.S. persons have the authority to control all substantial decisions of the trust or (y) has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person.

If a partnership (including any entity or arrangement treated as a partnership for U.S. federal income tax purposes) acquires our common stock, the tax treatment of a partner in the partnership will generally depend upon the status of the partner and the activities of the partnership. Persons who are partners of partnerships holding our common stock are urged to consult their tax advisors.

Distributions

Subject to the discussion below, distributions, if any, made to a Non-U.S. Holder of our common stock out of our current or accumulated earnings and profits generally will constitute dividends for U.S. tax purposes and will be subject to withholding tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty. To obtain a reduced rate of withholding under a treaty, a Non-U.S. Holder generally will be required to provide us with a properly-executed IRS Form W-8BEN, or other appropriate form, certifying the Non-U.S. Holder s entitlement to benefits under that treaty. Treasury regulations provide special rules to determine whether, for purposes of determining the applicability of a tax treaty, dividends paid to a Non-U.S. Holder that is an entity should be treated as paid to the entity or to those holding an interest in that entity. If a Non-U.S. Holder holds stock through a financial institution or other agent acting on the holder s behalf, the holder will be required to provide appropriate documentation to such agent. The holder s agent will then be required to provide certification to us or our paying agent, either directly or through other intermediaries.

We generally are not required to withhold tax on dividends paid to a Non-U.S. Holder that are effectively connected with the Non-U.S. Holder s conduct of a trade or business within the United States if a properly-executed IRS Form W-8ECI, stating that the dividends are so connected (and are not exempt from net U.S. federal income tax under a treaty as described below), is filed with us. Effectively connected dividends will be subject to net U.S.

Table of Contents

federal income tax, generally in the same manner and at the regular rate as if the Non-U.S. Holder were a U.S. citizen or resident alien or a domestic corporation, as the case may be, unless a specific treaty exemption applies. If the Non-U.S. Holder is eligible for the benefits of a tax treaty between the United States and the holder s country of residence, any effectively connected dividends would generally be subject to net U.S. federal income tax only if they are also attributable to a permanent establishment maintained by the holder in the United States. A corporate Non-U.S. Holder receiving effectively connected dividends may also be subject to an additional branch profits tax , which is imposed, under certain circumstances, at a rate of 30% (or such lower rate as may be specified by an applicable treaty) of the corporate Non-U.S. Holder s effectively connected earnings and profits, subject to certain adjustments. If you are eligible for a reduced rate of withholding tax pursuant to a tax treaty, you may generally obtain a refund of any excess amounts currently withheld if you timely file an appropriate claim for refund with the IRS.

To the extent distributions on our common stock, if any, exceed our current and accumulated earnings and profits, they will constitute a return of capital and will first reduce your basis in our common stock, but not below zero, and then will be treated as gain from the sale of stock.

Gain on disposition of common stock

A Non-U.S. Holder generally will not be subject to U.S. federal income tax with respect to gain realized on a sale or other disposition of our common stock unless (i) the gain is effectively connected with a trade or business of such holder in the United States, (ii) in the case of Non-U.S. Holders who are nonresident alien individuals, such individuals are present in the United States for 183 or more days in the taxable year of the disposition and certain other conditions are met, or (iii) we are or have been a United States real property holding corporation within the meaning of Code Section 897(c)(2) at any time within the shorter of the five-year period preceding such disposition or such holder s holding period. In general, we would be a United States real property holding corporation if interests in U.S. real estate comprised at least half of our business assets. We believe that we are not, and do not anticipate becoming, a United States real property holding corporation. Even if we are treated as a United States real property holding corporation, gain realized by a Non-U.S. Holder on a disposition of our common stock will not be subject to U.S. federal income tax so long as (1) the Non-U.S. Holder owned directly, indirectly and constructively, no more than five percent of our common stock at all times within the shorter of (a) the five year period preceding the disposition or (b) the holder s holding period and (2) our common stock is regularly traded on an established securities market. There can be no assurance that our common stock will continue to qualify as regularly traded on an established securities market.

If you are a Non-U.S. Holder described in (i) above, you will be required to pay tax on the net gain derived from the sale at generally applicable United States federal income tax rates, subject to an applicable income tax treaty providing otherwise, and corporate Non-U.S. Holders described in (i) above may be subject to the branch profits tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty. If you are an individual Non-U.S. Holder described in (ii) above, you will be required to pay a flat 30% tax (or a reduced rate under an applicable income tax treaty) on the gain derived from the sale, which tax may be offset by U.S. source capital losses if you have timely filed tax returns with respect to such losses (even though you are not considered a resident of the United States).

Information reporting and backup withholding

Generally, we must report to the IRS the amount of dividends paid, the name and address of the recipient, and the amount, if any, of tax withheld. A similar report is sent to the holder. Pursuant to tax treaties or certain other agreements, the IRS may make its reports available to tax authorities in the recipient s country of residence. Backup withholding will generally not apply to payments of dividends made by us or our paying agents to a Non-U.S. Holder if the holder has provided its federal taxpayer identification number, if any, or the required certification that it is not a U.S. person (which is generally provided by furnishing a properly-executed IRS Form W-8BEN), unless the payer otherwise has knowledge or reason to know that the payee is a U.S. person. The backup withholding rate is currently 28% and scheduled to rise to 31% after December 31, 2010. Backup withholding is generally not required on payments to corporations, whether domestic or foreign.

Under current U.S. federal income tax law, information reporting and backup withholding will apply to the proceeds of a disposition of our common stock effected by or through a U.S. office of a broker unless the disposing

Table of Contents

holder certifies as to its non-U.S. status or otherwise establishes an exemption. The certification procedures for claiming benefits under a tax treaty described in Distributions above will satisfy the certification requirements to avoid backup withholding as well. Generally, U.S. information reporting and backup withholding will not apply to a payment of disposition proceeds where the transaction is effected outside the United States through a non-U.S. office of a non-U.S. broker. Backup withholding will apply to a payment of disposition proceeds if the broker has actual knowledge or reason to know that the holder is a U.S. person.

Backup withholding is not an additional tax. Rather, the tax liability of persons subject to backup withholding will be reduced by the amount of tax withheld. If withholding results in an overpayment of taxes, a refund may generally be obtained, provided that the required information is timely furnished to the IRS.

New legislation relating to foreign accounts

Newly enacted legislation may impose withholding taxes on certain types of payments made to foreign financial institutions (as specifically defined in this new legislation) and certain other non-U.S. entities (including financial intermediaries). Under this legislation, the failure to comply with additional certification, information reporting and other specified requirements could result in withholding tax being imposed on payments of dividends and sales proceeds to foreign intermediaries and certain Non-U.S. Holders. The legislation imposes a 30% withholding tax on dividends, or gross proceeds from the sale or other disposition of, common stock paid to a foreign financial institution or to a foreign non-financial entity, unless (i) the foreign financial institution undertakes certain diligence and reporting obligations or (ii) the foreign non-financial entity either certifies it does not have any substantial United States owners or furnishes identifying information regarding each substantial United States owner. If the payee is a foreign financial institution, it must enter into an agreement with the United States Treasury requiring, among other things, that it undertake to identify accounts held by certain United States persons or United States-owned foreign entities, annually report certain information about such accounts, and withhold 30% on payments to account holders whose actions prevent it from complying with these reporting and other requirements. The legislation applies to payments made after December 31, 2012. Prospective investors should consult their tax advisors regarding this legislation.

Federal estate tax

An individual who at the time of death is not a citizen or resident of the United States and who is treated as the owner of, or has made certain lifetime transfers of, an interest in our common stock will be required to include the value thereof in his or her taxable estate for U.S. federal estate tax purposes, and may be subject to U.S. federal estate tax unless an applicable estate tax treaty provides otherwise. The U.S. federal estate tax was automatically repealed effective January 1, 2010, for the estates of decedents dying in the year 2010. Accordingly, at present, there is no U.S. federal estate tax. However, Congress could pass a law reinstating the estate tax that has retroactive effect. In addition, unless Congress acts to make the current repeal permanent, the estate tax will be reinstated with respect to decedents who die after December 31, 2010. The test for whether an individual is a resident of the United States for federal estate tax purposes differs from the test used for U.S. federal income tax purposes. Some individuals, therefore, may be Non-U.S. Holders for U.S. federal income tax purposes, but not for U.S. federal estate tax purposes, and vice versa.

THE PRECEDING DISCUSSION OF U.S. FEDERAL INCOME TAX CONSIDERATIONS IS FOR GENERAL INFORMATION ONLY. IT IS NOT TAX ADVICE. EACH PROSPECTIVE INVESTOR SHOULD CONSULT ITS OWN TAX ADVISOR REGARDING THE TAX CONSEQUENCES OF PURCHASING, HOLDING AND DISPOSING OF OUR COMMON STOCK, INCLUDING THE CONSEQUENCES OF ANY PROPOSED CHANGE IN APPLICABLE LAW.

Table of Contents

UNDERWRITING

Under the terms and subject to the conditions in an underwriting agreement dated the date of this prospectus supplement, the underwriter named below has agreed to purchase, and we have agreed to sell to it, the number of shares of our common stock at the public offering price, less the underwriting discounts and commissions, as set forth on the cover page of this prospectus supplement as indicated below:

Underwriter	Number of Shares
Lazard Capital Markets LLC	14,285,715
Total	14,285,715

The underwriter is offering the shares of common stock subject to its acceptance of the shares from us and subject to prior sale. The underwriting agreement provides that the obligations of the underwriter to pay for and accept delivery of the shares offered by this prospectus supplement are subject to certain conditions precedent, including the absence of any material adverse change in our business and the approval of certain legal matters by its counsel and the receipt of customary legal opinions, letters and certificates and to other conditions. The underwriter is obligated to take and pay for all of the shares of common stock offered by this prospectus supplement if any such shares are taken.

The underwriter has an option to buy up to 2,142,857 additional shares of common stock from us to cover sales of shares by the underwriter which exceed the number of shares specified in the table above. The underwriter may exercise this option at any time and from time to time during the 30-day period from the date of this prospectus supplement. If any additional shares of common stock are purchased, the underwriter will offer the additional shares of common stock on the same terms as those on which the shares are being offered.

The underwriter initially proposes to offer the shares of common stock directly to the public at the public offering price listed on the cover page of this prospectus supplement. After the initial offering of the shares, the offering price and other selling terms may from time to time be varied by the underwriter.

Commissions and Discounts

The following table summarizes the public offering price, underwriting discount and proceeds before expenses to us assuming both no exercise and full exercise of the underwriter s option to purchase additional shares of common stock:

		Total	
	Per Share	Without Over-Allotment	With Over-Allotment
Public offering price	$ 2.80	$ 40,000,002	$ 46,000,002
Underwriting discounts and commissions	0.14	2,000,000	2,300,000
Proceeds, before expenses, to us	2.66	38,000,002	43,700,002

The expenses of the offering, not including the underwriting discount and commissions, payable by us are estimated to be $375,000.

The relationship between Lazard Frères & Co. LLC and Lazard Capital Markets LLC is governed by a business alliance agreement between their respective parent companies. Pursuant to such agreement, Lazard Frères & Co. LLC referred this offering to Lazard Capital Markets LLC and will receive a referral fee from Lazard Capital Markets LLC in connection therewith; however, such referral fee is not in addition to the fee paid by us to Lazard Capital Markets LLC described above.

Table of Contents

Quotation on the NASDAQ Global Market

Our common stock is listed on The NASDAQ Global Market under the symbol GTXI. Our registrar and transfer agent for our common stock is Computershare Trust Company, N.A., located at 150 Royall Street, Canton, MA 02021.

Indemnification

We and the underwriter have agreed to indemnify each other, and we have also agreed to indemnify Lazard Frères & Co. LLC, against certain liabilities, including liabilities under the Securities Act and liabilities arising from breaches of representations and warranties contained in the underwriting agreement. We have also agreed to contribute to payments the underwriter and Lazard Frères & Co. LLC may be required to make in respect of such liabilities.

Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers or persons controlling the registrant pursuant to the foregoing provisions, the registrant has been informed that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is therefore unenforceable.

No Sales of Similar Securities

We and each of our executive officers and directors have agreed with the underwriter, subject to certain exceptions, not to dispose of or hedge any of our shares of common stock or securities convertible into or exercisable or exchangeable for common stock for 90 days after the date of this prospectus supplement without first obtaining the written consent of Lazard Capital Markets LLC. Exceptions to these lock-up agreements with our directors and executive officers include the following: (i) transfers to any member of the immediate family of the party to the lock-up from or by a grantor retained (or like-kind) annuity trust which exists as of the date of this prospectus supplement and was established for the direct or indirect benefit of the undersigned and/or any member of the immediate family of the undersigned pursuant to the terms of such trust, (ii) transfers in the event of a default under a pledge which exists as of the date hereof as security for a margin or loan account pursuant to the terms of such account, (iii) transfers pursuant to any Rule 10b5-1 trading plans in effect as of the date of the date of this offering, and (iv) from and after the date that is 45 days following the date of this prospectus supplement, open market sales of up to, in the aggregate, 10,000 shares of our common stock for each of our directors and executive officers. Exceptions to the lock-up agreement with us include our ability to issue shares of our common stock or securities convertible into or exercisable or exchangeable for our common stock at any time in connection with strategic transactions involving us and other entities. The 90-day lock-up period during which we and our executive officers and directors are restricted from engaging in transactions in our common stock or securities convertible into or exercisable or exchangeable for common stock is subject to extension in the event that either (i) during the last 17 days of the lock-up period, we issue an earnings or financial results release or material news or a material event relating to us occurs, or (ii) prior to the expiration of the lock-up period, we announce that we will release earnings or financial results during the 16-day period beginning on the last day of the lock-up period, then in either case the expiration of the lock-up period will be extended until the expiration of the 18-day period beginning on the issuance of the earnings or financial results release or the occurrence of the material news or material event, as applicable, unless Lazard Capital Markets LLC waives, in writing, such an extension.

Price Stabilization, Short Positions

In order to facilitate the offering of the shares of common stock, the underwriter may engage in transactions that stabilize, maintain or otherwise affect the price of our common stock. Specifically, the underwriter may sell more shares of common stock than it is obligated to purchase under the underwriting agreement, creating a short position. The underwriter must close out any short position by purchasing shares of common stock in the open market. A short position may be created if the underwriter is concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchased in this offering. As an additional means of facilitating this offering, the underwriter may bid for, and purchase, shares of our common stock in the open market to stabilize the price of the common stock. These activities may raise or maintain the market price of our common stock above independent market levels or prevent or slow a decline in the market price of our common stock. The underwriter is not required to engage in these activities, and may end any of these activities at any

time.

Table of Contents

A prospectus in electronic format may be made available on websites maintained by the underwriter. Internet distributions will be allocated by the underwriter on the same basis as other allocations.

United Kingdom

This document is only being distributed to and is only directed at (i) persons who are outside the United Kingdom or (ii) to investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (the Order) or (iii) high net worth entities, and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (e) of the Order (all such persons together being referred to as relevant persons). The shares of common stock are only available to, and any invitation, offer or agreement to subscribe, purchase or otherwise acquire such shares will be engaged in only with, relevant persons. Any person who is not a relevant person should not act or rely on this document or any of its contents.

Each underwriter has represented and agreed that:

(a) it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act 2000 or FSMA) received by it in connection with the issue or sale of the shares in circumstances in which Section 21(1) of the FSMA does not apply to us, and

(b) it has complied with, and will comply with all applicable provisions of FSMA with respect to anything done by it in relation to the shares in, from or otherwise involving the United Kingdom.

European Economic Area

To the extent that the offer of the shares of common stock are made in any Member State of the European Economic Area that has implemented the Prospectus Directive before the date of publication of a prospectus in relation to the shares of common stock which has been approved by the competent authority in the Member State in accordance with the Prospectus Directive (or, where appropriate, published in accordance with the Prospectus Directive and notified to the competent authority in the Member State in accordance with the Prospectus Directive), the offer (including any offer pursuant to this document) is only addressed to qualified investors in that Member State within the meaning of the Prospectus Directive or has been or will be made otherwise in circumstances that do not require us to publish a prospectus pursuant to the Prospectus Directive.

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State), each underwriter has represented and agreed that with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State (the Relevant Implementation Date) it has not made and will not make an offer of shares to the public in that Relevant Member State prior to the publication of a prospectus in relation to the shares which has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the competent authority in that Relevant Member State, all in accordance with the Prospectus Directive, except that it may, with effect from and including the Relevant Implementation Date, make an offer of shares to the public in that Relevant Member State at any time:

(a) to legal entities which are authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities,

(b) to any legal entity which has two or more of (1) an average of at least 250 employees during the last financial year; (2) a total balance sheet of more than 43,000,000 and (3) an annual net turnover of more than 50,000,000, as shown in its last annual or consolidated accounts, or

(c) in any other circumstances which do not require the publication by us of a prospectus pursuant to Article 3 of the Prospectus Directive. For the purposes of this provision, the expression an offer of shares to the public in relation to any shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the shares to be offered so as to enable an investor to decide to purchase or subscribe the shares, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State and

Table of Contents

the expression Prospectus Directive means Directive 2003/71/EC and includes any relevant implementing measure in each Relevant Member State.

The EEA selling restriction is in addition to any other selling restrictions set out below. In relation to each Relevant Member State, each purchaser of shares of common stock (other than the underwriter) will be deemed to have represented, acknowledged and agreed that it will not make an offer of shares of common stock to the public in any Relevant Member State, except that it may, with effect from and including the date on which the Prospectus Directive is implemented in the Relevant Member State, make an offer of shares of common stock to the public in that Relevant Member State at any time in any circumstances which do not require the publication by us of a prospectus pursuant to Article 3 of the Prospectus Directive, provided that such purchaser agrees that it has not and will not make an offer of any shares of common stock in reliance or purported reliance on Article 3(2)(b) of the Prospectus Directive. For the purposes of this provision, the expression an offer of Shares to the public in relation to any shares of common stock in any Relevant Member State has the same meaning as in the preceding paragraph.

Table of Contents

LEGAL MATTERS

Cooley LLP, Palo Alto, California will pass upon the validity of the issuance of the common stock offered by this prospectus supplement and the accompanying prospectus. Certain legal matters will be passed upon for the underwriter by Proskauer Rose LLP, New York, New York.

EXPERTS

The financial statements of GTx, Inc. appearing in GTx, Inc. s Annual Report (Form 10-K) for the year ended December 31, 2009, and the effectiveness of GTx, Inc. s internal control over financial reporting as of December 31, 2009, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their reports thereon, included therein, and incorporated herein by reference. Such financial statements are, and audited financial statements to be included in subsequently filed documents will be, incorporated herein in reliance upon the reports of Ernst & Young LLP pertaining to such financial statements and the effectiveness of our internal control over financial reporting as of the respective dates (to the extent covered by consents filed with the SEC) given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the reporting requirements of the Exchange Act and we file annual, quarterly and special reports, proxy statements and other information with the SEC. You may read and copy any document we file at the SEC s Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the Public Reference Room. The SEC maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC, including GTx, Inc. The SEC s Internet site can be found at *www.sec.gov*. Our common stock is listed on The NASDAQ Global Market, and you can read and inspect our filings at the offices of The NASDAQ Stock Market at 1735 K Street, Washington, D.C. 20006. We maintain a website at www.gtxinc.com. The information contained on our website is not incorporated by reference in this prospectus supplement and the accompanying prospectus and you should not consider it a part of this prospectus supplement and the accompanying prospectus.

You should rely only on the information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus, along with the information contained in any free writing prospectus that we have authorized for use in connection with this offering. We have not authorized anyone to provide you with different or additional information. We are not making an offer of these securities in any state where the offer is not permitted. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and in any free writing prospectus that we have authorized for use in connection with this offering is accurate only as of the respective dates of those documents. Our business, financial condition, results of operations and prospects may have changed since those dates.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference information from other documents that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus supplement and the accompanying prospectus. Information contained in this prospectus supplement and the accompanying prospectus and information that we file with the SEC in the future and incorporate by reference in this prospectus supplement and the accompanying prospectus will automatically update and supersede this information. We incorporate by reference the documents listed below and any future filings (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items) we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, after the date of the prospectus supplement and prior to the termination of the offering of the common stock covered by this prospectus supplement (Commission File No. 0-50549):

- our Annual Report on Form 10-K for the year ended December 31, 2009, filed with the SEC on March 15, 2010;

Table of Contents

the information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2009 from our definitive proxy statement on Schedule 14A for our 2010 Annual Meeting of Stockholders, filed with the SEC on March 18, 2010;

our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2010 and June 30, 2010, filed with the SEC on May 4, 2010 and August 9, 2010, respectively;

our Current Reports on Form 8-K filed with the SEC on February 19, 2010, March 9, 2010, March 15, 2010 (except for the information furnished under Item 2.02 and the related exhibit), March 23, 2010, March 26, 2010, May 4, 2010 (except for the information furnished under Item 2.02 and the related exhibit), May 26, 2010, June 9, 2010, June 21, 2010, September 15, 2010, October 26, 2010 and October 27, 2010; and

the description of our common stock contained in our registration statement on Form 8-A filed with the SEC on January 13, 2004, including all amendments and reports filed for the purpose of updating such information.

We will furnish without charge to you, upon written or oral request, a copy of any or all of the documents incorporated by reference, including exhibits to these documents. You should direct any requests for documents to GTx, Inc., Attention: Corporate Secretary, 175 Toyota Plaza, Suite 700, Memphis, Tennessee 38103. Our phone number is (901) 523-9700.

Table of Contents

PROSPECTUS

$100,000,000
Common Stock
Preferred Stock
Debt Securities
Warrants
Units

From time to time, we may offer up to $100,000,000 of any combination of the securities described in this prospectus, either individually or in units. We may also offer common stock or preferred stock upon conversion of debt securities, common stock upon conversion of preferred stock, or common stock, preferred stock or debt securities upon the exercise of warrants.

We will provide the specific terms of these offerings and securities in one or more supplements to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. The prospectus supplement and any related free writing prospectus may also add, update or change information contained in this prospectus. You should carefully read this prospectus, the applicable prospectus supplement and any related free writing prospectus, as well as any documents incorporated by reference, before buying any of the securities being offered.

Our common stock is traded on the NASDAQ Global Market under the symbol GTXI. On December 24, 2007, the last reported sale price of our common stock on the NASDAQ Global Market was $15.23. The applicable prospectus supplement will contain information, where applicable, as to any other listing, if any, on the NASDAQ Global Market or any securities market or other exchange of the securities covered by the applicable prospectus supplement.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading Risk Factors contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus.

This prospectus may not be used to consummate a sale of any securities unless accompanied by a prospectus supplement.

The securities may be sold directly by us to investors, through agents designated from time to time or to or through underwriters or dealers, on a continuous or delayed basis. For additional information on the methods of sale, you should refer to the section entitled Plan of Distribution in this prospectus. If any agents or underwriters are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such agents or underwriters and any applicable fees, commissions, discounts and over-allotment options will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds that we expect to receive from such sale will also be set forth in a prospectus supplement.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is January 17, 2008.

TABLE OF CONTENTS

Table of Contents

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission utilizing a shelf registration process. Under this shelf registration process, we may offer shares of our common stock and preferred stock, various series of debt securities and/or warrants to purchase any of such securities, either individually or in units, in one or more offerings, up to a total dollar amount of $100,000,000. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will contain more specific information about the terms of those securities. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. We may also add, update or change in the prospectus supplement (and in any related free writing prospectus that we may authorize to be provided to you) any of the information contained in this prospectus or in the documents that we have incorporated by reference into this prospectus. We urge you to carefully read this prospectus, any applicable prospectus supplement and any related free writing prospectus, together with the information incorporated herein by reference as described under the heading Where You Can Find Additional Information, before buying any of the securities being offered. **THIS PROSPECTUS MAY NOT BE USED TO CONSUMMATE A SALE OF SECURITIES UNLESS IT IS ACCOMPANIED BY A PROSPECTUS SUPPLEMENT.**

You should rely only on the information that we have provided or incorporated by reference in this prospectus, any applicable prospectus supplement and any related free writing prospectus that we may authorize to be provided to you. We have not authorized anyone to provide you with different information. No dealer, salesperson or other person is authorized to give any information or to represent anything not contained in this prospectus, any applicable prospectus supplement or any related free writing prospectus that we may authorize to be provided to you. You must not rely on any unauthorized information or representation. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should assume that the information in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate only as of the date on the front of the document and that any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus, any applicable prospectus supplement or any related free writing prospectus, or any sale of a security.

This prospectus contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described below under the heading Where You Can Find Additional Information.

Table of Contents

This prospectus and the information incorporated herein by reference includes trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included or incorporated by reference into this prospectus, any applicable prospectus supplement or any related free writing prospectus are the property of their respective owners.

Unless otherwise mentioned or unless the context requires otherwise, all references in this prospectus to GTx, we, our or similar references mean GTx, Inc.

GTx, INC.

We are a biopharmaceutical company dedicated to the discovery, development and commercialization of small molecules that selectively target hormone pathways to treat cancer, osteoporosis and bone loss, muscle wasting and other serious medical conditions. We are developing ACAPODENE (toremifene citrate), a selective estrogen receptor modulator, or SERM, in two separate clinical programs in men: first, a pivotal Phase III clinical trial for the treatment of multiple serious side effects of androgen deprivation therapy for advanced prostate cancer, and second, a pivotal Phase III clinical trial for the prevention of prostate cancer in high risk men with precancerous prostate lesions called high grade prostatic intraepithelial neoplasia. We have licensed to Ipsen Limited exclusive rights in the European Union, Switzerland, Norway, Iceland, Lichtenstein and the Commonwealth of Independent States to develop and commercialize ACAPODENE and other products containing toremifene in all indications that we have licensed from Orion Corporation, which include all indications in humans except the treatment and prevention of breast cancer outside of the United States. We are also developing Ostarine, a selective androgen receptor modulator, or SARM, which is currently being evaluated in a Phase II clinical trial for the treatment of muscle loss in patients with cancer. We have entered into an exclusive license and collaboration agreement with Merck & Co., Inc., or Merck, governing our and Merck s joint research, development and global commercialization of SARMs with the potential to treat age-related muscle loss (sarcopenia) as well as other musculoskeletal conditions. We also have an extensive preclinical pipeline generated from our own discovery program. We are evolving into a selective nuclear hormone receptor modulator company that develops small molecules to target hormone pathways to address a myriad of unmet medical needs in men and women.

We plan to build specialized sales and marketing capabilities to promote our product candidates to urologists and medical oncologists in the United States and to seek additional partners to commercialize our product candidates in broader markets in the United States and in the rest of the world. We currently market FARESTON (toremifene citrate 60 mg) tablets, which have been approved by the U.S. Food and Drug Administration, or FDA, for the treatment of metastatic breast cancer in postmenopausal women in the United States. The active pharmaceutical ingredient in FARESTON is the same as in ACAPODENE, but at a different dose.

We have a limited operating history and may not be able to attain profitability. We have financed our operations and internal growth primarily through private placements of preferred stock and our public offerings of common stock. We have incurred losses in each year since our inception in 1997 and we expect to continue to incur net losses over the next several years as we continue our clinical development and research and development activities, apply for regulatory approvals, expand our sales and marketing capabilities and grow our operations.

We were originally incorporated under the name Genotherapeutics, Inc. in Tennessee in September 1997. We changed our name to GTx, Inc. in 2001, and we reincorporated in Delaware in 2003. Our principal executive office is located at 3 N. Dunlap Street, Van Vleet Building, Memphis, Tennessee, and our telephone number is (901) 523-9700. Our website address is www.gtxinc.com. The information contained in, or that can be accessed through, our website is not part of this prospectus.

RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully review the risks and uncertainties described under the heading Risk Factors contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus. Additional risks not presently known to us or that we currently believe are immaterial may also significantly impair our business operations.

FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be

Table of Contents

materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. Forward-looking statements include statements about:

- the anticipated progress of our and our collaborators research, development and clinical programs, including whether future clinical trials will achieve similar results to clinical trials that we have successfully concluded;
- potential future licensing fees, milestone payments and royalty payments, including any milestone payments or royalty payments that we may receive under our collaborative arrangements with Ipsen Limited and Merck & Co., Inc.;
- our and our collaborators ability to market, commercialize and achieve market acceptance for our product candidates or products that we and/or our collaborators may develop;
- our and our collaborators ability to generate additional product candidates for clinical testing;
- our ability to protect our intellectual property and operate our business without infringing upon the intellectual property rights of others; and
- our estimates regarding the sufficiency of our cash resources.

In some cases, you can identify forward-looking statements by terms such as anticipates, believes , could , estimate expects , intends , may , plans , potential , predicts , projects , should , will , would and similar express identify forward-looking statements. Forward-looking statements reflect our current views with respect to future events, are based on assumptions and are subject to risks, uncertainties and other important factors. We discuss many of these risks, uncertainties and other important factors in greater detail under the heading Risk Factors contained in the applicable prospectus supplement and any related free writing prospectus, and in our most recent annual report on Form 10-K and in our most recent quarterly report on Form 10-Q, as well as any amendments thereto reflected in subsequent filings with the SEC. Given these risks, uncertainties and other important factors, you should not place undue reliance on these forward-looking statements. Also, these forward-looking statements represent our estimates and assumptions only as of the date such forward-looking statements are made. You should carefully read this prospectus, the applicable prospectus supplement and any related free writing prospectus, together with the information incorporated herein by reference as described under the heading Where You Can Find Additional Information, completely and with the understanding that our actual future results may be materially different from what we expect.

Except as required by law, we assume no obligation to update any forward-looking statements publicly, or to update the reasons why actual results could differ materially from those anticipated in any forward-looking statements, even if new information becomes available in the future.

THE SECURITIES WE MAY OFFER

We may offer shares of our common stock and preferred stock, various series of debt securities and/or warrants to purchase any of such securities, either individually or in units, with a total value of up to $100,000,000 from time to time under this prospectus at prices and on terms to be determined by market conditions at the time of any offering. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

- designation or classification;
- aggregate principal amount or aggregate offering price;
- maturity, if applicable;
- original issue discount, if any;

rates and times of payment of interest or dividends, if any;

redemption, conversion, exercise, exchange or sinking fund terms, if any;

ranking;

restrictive covenants, if any;

Table of Contents

voting or other rights, if any;

conversion prices, if any; and

important United States federal income tax considerations.

The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in documents we have incorporated by reference. However, no prospectus supplement or free writing prospectus will offer a security that is not registered and described in this prospectus at the time of the effectiveness of the registration statement of which this prospectus is a part.

THIS PROSPECTUS MAY NOT BE USED TO CONSUMMATE A SALE OF SECURITIES UNLESS IT IS ACCOMPANIED BY A PROSPECTUS SUPPLEMENT.

We may sell the securities directly to investors or to or through agents, underwriters or dealers. We, and our agents or underwriters, reserve the right to accept or reject all or part of any proposed purchase of securities. If we do offer securities to or through agents or underwriters, we will include in the applicable prospectus supplement:

the names of those agents or underwriters;

applicable fees, discounts and commissions to be paid to them;

details regarding over-allotment options, if any; and

the net proceeds to us.

Common Stock. We may issue shares of our common stock from time to time. The holders of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of stockholders and do not have cumulative voting rights. Subject to preferences that may be applicable to any outstanding shares of preferred stock, the holders of our common stock are entitled to receive ratably such dividends as may be declared by our board of directors out of legally available funds. Upon our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preferences of any outstanding shares of preferred stock.

Preferred Stock. We may issue shares of our preferred stock from time to time, in one or more series. Our board of directors will determine the designations, voting powers, preferences and rights of the preferred stock, as well as the qualifications, limitations or restrictions thereof, including dividend rights, conversion rights, preemptive rights, terms of redemption or repurchase, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of any series. Convertible preferred stock will be convertible into our common stock or exchangeable for our other securities. Conversion may be mandatory or at your option and would be at prescribed conversion rates.

If we sell any series of preferred stock under this prospectus, we will fix the designations, voting powers, preferences and rights of such series of preferred stock, as well as the qualifications, limitations or restrictions thereof, in the certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that describes the terms of the series of preferred stock that we are offering before the issuance of the related series of preferred stock. We urge you to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the series of preferred stock being offered, as well as the complete certificate of designation that contains the terms of the applicable series of preferred stock.

Debt Securities. We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. The senior debt securities will rank equally with any other unsecured and unsubordinated debt. The subordinated debt securities will be subordinate and junior in right of payment, to the extent and in the manner described in the instrument governing the debt, to all of our senior

indebtedness. Convertible debt securities will be convertible into or exchangeable for our common stock or our other securities. Conversion may be mandatory or at your option and would be at prescribed conversion rates.

Table of Contents

The debt securities will be issued under one or more documents called indentures, which are contracts between us and a national banking association or other eligible party, as trustee. In this prospectus, we have summarized certain general features of the debt securities. We urge you, however, to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the series of debt securities being offered, as well as the complete indentures that contain the terms of the debt securities. Forms of indentures have been filed as exhibits to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

Warrants. We may issue warrants for the purchase of common stock, preferred stock and/or debt securities in one or more series. We may issue warrants independently or together with common stock, preferred stock and/or debt securities, and the warrants may be attached to or separate from these securities. In this prospectus, we have summarized certain general features of the warrants. We urge you, however, to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the particular series of warrants being offered, as well as the complete warrant agreements and warrant certificates that contain the terms of the warrants. Forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants being offered have been filed as exhibits to the registration statement of which this prospectus is a part, and supplemental warrant agreements and forms of warrant certificates will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

We will evidence each series of warrants by warrant certificates that we will issue. Warrants may be issued under an applicable warrant agreement that we enter into with a warrant agent. We will indicate the name and address of the warrant agent, if applicable, in the prospectus supplement relating to the particular series of warrants being offered.

Units. We may issue, in one or more series, units consisting of common stock, preferred stock, debt securities and/or warrants for the purchase of common stock, preferred stock and/or debt securities in any combination. In this prospectus, we have summarized certain general features of the units. We urge you, however, to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the series of units being offered, as well as the complete unit agreement that contains the terms of the units. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of unit agreement and any supplemental agreements that describe the terms of the series of units we are offering before the issuance of the related series of units.

We will evidence each series of units by unit certificates that we will issue. Units may be issued under a unit agreement that we enter into with a unit agent. We will indicate the name and address of the unit agent, if applicable, in the prospectus supplement relating to the particular series of units being offered.

RATIO OF EARNINGS TO FIXED CHARGES

Our earnings were insufficient to cover fixed charges for each of the periods presented. Accordingly, the following table sets forth the deficiency of earnings to fixed charges for each of the periods presented. Because of the deficiency, ratio information is not applicable. Amounts shown are in thousands.

	Nine Months Ended September 30,	Year Ended December 31,				
	2007	2006	2005	2004	2003	2002
Deficiency of earnings available to cover fixed charges	$ (27,569)	$(35,510)	$(36,839)	$(22,348)	$(14,194)	$(11,866)

For purposes of computing the deficiency of earnings available to cover fixed charges, fixed charges represent that portion of rental expense that is considered by us to be representative of interest. Earnings consists of loss before income taxes plus fixed charges.

USE OF PROCEEDS

Except as described in any prospectus supplement or in any related free writing prospectus that we may authorize to be provided to you, we currently intend to use the net proceeds from the sale of the securities offered hereby for research and development and general corporate purposes. We may also use a portion of the net proceeds to acquire or invest in businesses, products and technologies that are complementary to our own, as well as for capital expenditures. Pending these uses, we expect to invest the net proceeds in short-term, investment-grade securities.

Table of Contents

DESCRIPTION OF CAPITAL STOCK

General

Our authorized capital stock consists of 60,000,000 shares of common stock, $0.001 par value per share, and 5,000,000 shares of preferred stock, $0.001 par value per share. As of December 18, 2007, there were 36,216,263 shares of our common stock outstanding and no shares of preferred stock outstanding.

The following summary description of our capital stock is based on the provisions of our certificate of incorporation and bylaws and the applicable provisions of the Delaware General Corporation Law. This information is qualified entirely by reference to the applicable provisions of our certificate of incorporation, bylaws and the Delaware General Corporation Law. For information on how to obtain copies of our certificate of incorporation and bylaws, which are exhibits to the registration statement of which this prospectus is a part, see Where You Can Find Additional Information.

Common Stock

The holders of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of stockholders. The holders of our common stock do not have cumulative voting rights in the election of directors. Subject to preferences that may be applicable to any outstanding shares of preferred stock, the holders of common stock are entitled to receive ratably such dividends as may be declared by our board of directors out of legally available funds. Upon our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preferences of any outstanding shares of preferred stock. Holders of common stock have no preemptive rights and no right to convert their common stock into any other securities. There are no redemption or sinking fund provisions applicable to our common stock.

The rights of the holders of our common stock are subject to, and may be adversely affected by, the rights of holders of shares of any preferred stock that we may designate and issue in the future.

Preferred Stock

Pursuant to our certificate of incorporation, our board of directors has the authority, without further action by the stockholders (unless such stockholder action is required by applicable law or NASDAQ rules), to designate and issue up to 5,000,000 shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each such series, to fix the designations, voting powers, preferences and rights of the shares of each wholly unissued series, and any qualifications, limitations or restrictions thereof, and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding.

We will fix the designations, voting powers, preferences and rights of the preferred stock of each series, as well as the qualifications, limitations or restrictions thereof, in the certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that describes the terms of the series of preferred stock we are offering before the issuance of that series of preferred stock. This description will include:

- the title and stated value;
- the number of shares we are offering;
- the liquidation preference per share;
- the purchase price;
- the dividend rate, period and payment date and method of calculation for dividends;
- whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- the procedures for any auction and remarketing, if any;

the provisions for a sinking fund, if any;

Table of Contents

the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;

any listing of the preferred stock on any securities exchange or market;

whether the preferred stock will be convertible into our common stock, and, if applicable, the conversion price, or how it will be calculated, and the conversion period;

whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price, or how it will be calculated, and the exchange period;

voting rights, if any, of the preferred stock;

preemptive rights, if any;

restrictions on transfer, sale or other assignment, if any;

whether interests in the preferred stock will be represented by depositary shares;

a discussion of any material United States federal income tax considerations applicable to the preferred stock;

the relative ranking and preferences of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;

any limitations on the issuance of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and

any other specific terms, preferences, rights or limitations of, or restrictions on, the preferred stock.

The General Corporation Law of the State of Delaware, the state of our incorporation, provides that the holders of preferred stock will have the right to vote separately as a class (or, in some cases, as a series) on an amendment to our certificate of incorporation if the amendment would change the par value or, unless the certificate of incorporation provided otherwise, the number of authorized shares of the class or change the powers, preferences or special rights of the class or series so as to adversely affect the class or series, as the case may be. This right is in addition to any voting rights that may be provided for in the applicable certificate of designation.

Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of our common stock. Preferred stock could be issued quickly with terms designed to delay or prevent a change in control of our company or make removal of management more difficult. Additionally, the issuance of preferred stock may have the effect of decreasing the market price of our common stock.

Registration Rights

J.R. Hyde, III, and Oracle Partners, L.P., two of our largest stockholders, and their affiliates, are entitled to certain rights with respect to the registration of approximately 10.9 million shares of our common stock under the Securities Act of 1933, based on shares held as of December 18, 2007. If we propose to register any of our securities under the Securities Act, either for our own account or for the account of others, the holders of these shares are entitled to notice of the registration and are entitled to include, at our expense, their shares of common stock in the registration and any related underwriting, provided, among other conditions, that the underwriters may limit the number of shares to be included in the registration. These holders have waived these registration rights in connection with the filing of, and any offerings that might be made pursuant to, the registration statement of which this prospectus is a part. In addition, the holders of these shares may require us, at our expense and subject to certain limitations, to file a registration

statement under the Securities Act with respect to their shares of our common stock. We have also entered into a registration rights agreement with Merck & Co., Inc., or Merck, pursuant to which we agreed to file and keep effective a shelf registration statement under the Securities Act registering the resale from time to time thereunder of the 1,285,347 shares of common stock that we issued to Merck in December 2007.

Anti-Takeover Effects of Provisions of Delaware Law and Our Charter Documents

Delaware Takeover Statute. We are subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, the statute prohibits a publicly-held Delaware corporation such as us 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,

Table of Contents

unless the business combination is approved in a prescribed manner. For purposes of Section 203, a business combination includes a merger, asset or stock sale or other transaction resulting in a financial benefit to the interested stockholder, and an interested stockholder is a person who, together with affiliates and associates, owns, or within three years prior, did own, 15% or more of our voting stock. Section 203 of the Delaware General Corporation Law will generally have an anti-takeover effect for transactions not approved in advance by our board of directors, including discouraging attempts that might result in a premium over the market price for the shares of common stock held by our stockholders.

Charter Documents. Our certificate of incorporation and bylaws provide that our board of directors be divided into three classes of directors, with each class serving a staggered three-year term. The classification system of electing directors may tend to discourage a third party from making a tender offer or otherwise attempting to obtain control of us and may maintain the composition of our current board of directors, as the classification of the board of directors generally increases the difficulty of replacing a majority of directors. In addition, our certificate of incorporation and bylaws:

- provide that any action required or permitted to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and may not be effected by any consent in writing;
- establish advance notice requirements for nominations for election to our board of directors or for proposing matters that can be acted upon at a stockholder meeting;
- provide that the authorized number of directors may be changed only by resolution of the board of directors; and
- provide that special meetings of our stockholders may be called only by the chairman of our board of directors, our chief executive officer or our board of directors pursuant to a resolution adopted by a majority of the total number of authorized directors.

The Delaware corporate law statute provides generally that the affirmative vote of a majority of the shares entitled to vote is required to amend a corporation s bylaws, unless a corporation s certificate of incorporation requires a greater percentage or also confers the power upon the corporation s directors. Our bylaws may be amended or repealed by:

- the affirmative vote of a majority of our directors then in office; or
- the affirmative vote of the holders of at least 66-2/3% of the voting power of all then-outstanding shares of our capital stock entitled to vote generally in the election of directors.

The provisions described in the preceding paragraph that are included in our certificate of incorporation may only be amended or repealed by the affirmative vote of a majority of our directors and the affirmative vote of the holders of at least 66-2/3% of the voting power of all then-outstanding shares of our capital stock entitled to vote generally in the election of directors.

These and other provisions contained in our certificate of incorporation and bylaws could delay or discourage some types of transactions involving an actual or potential change in our control or change in our management, including transactions in which stockholders might otherwise receive a premium for their shares over then current prices, and may limit the ability of stockholders to remove current management or approve transactions that stockholders may deem to be in their best interests and, therefore, could adversely affect the price of our common stock.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A. Its address is 150 Royall Street, Canton, MA 02021. The transfer agent for any series of preferred stock that we may offer under this prospectus will be named and described in the prospectus supplement for that series.

DESCRIPTION OF DEBT SECURITIES

We may issue debt securities, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. While the terms we have summarized below will apply generally to any debt securities that we may offer under this prospectus, we will describe the particular terms of any debt securities that we may offer

in more detail in the applicable prospectus supplement. The terms of any debt securities offered under a prospectus supplement may differ from the terms described below. Unless the context

Table of Contents

requires otherwise, whenever we refer to the indentures, we also are referring to any supplemental indentures that specify the terms of a particular series of debt securities.

We will issue the senior debt securities under the senior indenture that we will enter into with the trustee named in the senior indenture. We will issue the subordinated debt securities under the subordinated indenture that we will enter into with the trustee named in the subordinated indenture. The indentures will be qualified under the Trust Indenture Act of 1939. We use the term debenture trustee to refer to either the trustee under the senior indenture or the trustee under the subordinated indenture, as applicable. We have filed forms of indentures to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

The following summaries of material provisions of the senior debt securities, the subordinated debt securities and the indentures are subject to, and qualified in their entirety by reference to, all of the provisions of the indenture applicable to a particular series of debt securities. We urge you to read the applicable prospectus supplements and any related free writing prospectuses related to the debt securities that we may offer under this prospectus, as well as the complete indentures that contains the terms of the debt securities. Except as we may otherwise indicate, the terms of the senior indenture and the subordinated indenture are identical.

General

We will describe in the applicable prospectus supplement the terms of the series of debt securities being offered, including:

- the title;
- the principal amount being offered, and if a series, the total amount authorized and the total amount outstanding;
- any limit on the amount that may be issued;
- whether or not we will issue the series of debt securities in global form, the terms and who the depositary will be;
- the maturity date;
- whether and under what circumstances, if any, we will pay additional amounts on any debt securities held by a person who is not a United States person for tax purposes, and whether we can redeem the debt securities if we have to pay such additional amounts;
- the annual interest rate, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;
- whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;
- the terms of the subordination of any series of subordinated debt;
- the place where payments will be payable;
- restrictions on transfer, sale or other assignment, if any;
- our right, if any, to defer payment of interest and the maximum length of any such deferral period;

the date, if any, after which, and the price at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemption provisions;

the date, if any, on which, and the price at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder s option to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;

whether the indenture will restrict our ability and/or the ability of our subsidiaries to:

incur additional indebtedness;

issue additional securities;

create liens;

Table of Contents

pay dividends and make distributions in respect of our capital stock and the capital stock of our subsidiaries;

redeem capital stock;

place restrictions on our subsidiaries ability to pay dividends, make distributions or transfer assets;

make investments or other restricted payments;

sell or otherwise dispose of assets;

enter into sale-leaseback transactions;

engage in transactions with stockholders and affiliates;

issue or sell stock of our subsidiaries; or

effect a consolidation or merger;

whether the indenture will require us to maintain any interest coverage, fixed charge, cash flow-based, asset-based or other financial ratios;

a discussion of any material United States federal income tax considerations applicable to the debt securities;

information describing any book-entry features;

provisions for a sinking fund purchase or other analogous fund, if any;

the applicability of the provisions in the indenture on discharge;

whether the debt securities are to be offered at a price such that they will be deemed to be offered at an original issue discount as defined in paragraph (a) of Section 1273 of the Internal Revenue Code;

the denominations in which we will issue the series of debt securities, if other than denominations of $1,000 and any integral multiple thereof;

the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars; and

any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, including any additional events of default or covenants provided with respect to the debt securities, and any terms that may be required by us or advisable under applicable laws or regulations.

Conversion or Exchange Rights

We will set forth in the prospectus supplement the terms on which a series of debt securities may be convertible into or exchangeable for our common stock or our other securities. We will include provisions as to whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock or our other securities that the holders of the series of debt securities receive would be subject to adjustment.

Consolidation, Merger or Sale

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the indentures will not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of all or substantially all of our assets. However, any successor to or acquirer of such assets must assume all of our obligations under the indentures or the debt securities, as appropriate. If the debt securities are convertible into or exchangeable for our other securities or securities of other entities, the person with whom we consolidate or merge or to whom we sell all of our property must make provisions for the conversion of the debt securities into securities that the holders of the debt securities would have received if they had converted the debt securities before the consolidation, merger or sale.

Table of Contents

Events of Default Under the Indenture

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the following are events of default under the indentures with respect to any series of debt securities that we may issue:

- if we fail to pay interest when due and payable and our failure continues for 90 days and the time for payment has not been extended or deferred;
- if we fail to pay the principal, premium or sinking fund payment, if any, when due and payable and the time for payment has not been extended or delayed;
- if we fail to observe or perform any other covenant contained in the debt securities or the indentures, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive notice from the debenture trustee or holders of at least 25% in aggregate principal amount of the outstanding debt securities of the applicable series; and
- if specified events of bankruptcy, insolvency or reorganization occur.

If an event of default with respect to debt securities of any series occurs and is continuing, other than an event of default specified in the last bullet point above, the debenture trustee or the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series, by notice to us in writing, and to the debenture trustee if notice is given by such holders, may declare the unpaid principal of, premium, if any, and accrued interest, if any, due and payable immediately. If an event of default specified in the last bullet point above occurs with respect to us, the principal amount of and accrued interest, if any, of each issue of debt securities then outstanding shall be due and payable without any notice or other action on the part of the debenture trustee or any holder.

The holders of a majority in principal amount of the outstanding debt securities of an affected series may waive any default or event of default with respect to the series and its consequences, except defaults or events of default regarding payment of principal, premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Subject to the terms of the indentures, if an event of default under an indenture shall occur and be continuing, the debenture trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the debenture trustee reasonable indemnity. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the debenture trustee, or exercising any trust or power conferred on the debenture trustee, with respect to the debt securities of that series, provided that:

- the direction so given by the holder is not in conflict with any law or the applicable indenture; and
- subject to its duties under the Trust Indenture Act of 1939, the debenture trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

A holder of the debt securities of any series will have the right to institute a proceeding under the indentures or to appoint a receiver or trustee, or to seek other remedies only if:

- the holder has given written notice to the debenture trustee of a continuing event of default with respect to that series;
- the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made written request, and such holders have offered reasonable indemnity to the debenture trustee to institute the proceeding as trustee; and
- the debenture trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within

90 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities.

We will periodically file statements with the debenture trustee regarding our compliance with specified covenants in the indentures.

Table of Contents

Modification of Indenture; Waiver

We and the debenture trustee may change an indenture without the consent of any holders with respect to specific matters:

to fix any ambiguity, defect or inconsistency in the indenture;

to comply with the provisions described above under Description of Debt Securities Consolidation, Merger or Sale;

to comply with any requirements of the SEC in connection with the qualification of any indenture under the Trust Indenture Act of 1939;

to add to, delete from or revise the conditions, limitations, and restrictions on the authorized amount, terms, or purposes of issue, authentication and delivery of debt securities, as set forth in the indenture;

to provide for the issuance of and establish the form and terms and conditions of the debt securities of any series as provided under Description of Debt Securities General to establish the form of any certifications required to be furnished pursuant to the terms of the indenture or any series of debt securities, or to add to the rights of the holders of any series of debt securities;

to evidence and provide for the acceptance of appointment hereunder by a successor trustee;

to provide for uncertificated debt securities in addition to or in place of certificated debt securities and to make all appropriate changes for such purpose;

to add to our covenants such new covenants, restrictions, conditions or provisions for the protection of the holders, and to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default; or

to change anything that does not materially adversely affect the interests of any holder of debt securities of any series.

In addition, under the indentures, the rights of holders of a series of debt securities may be changed by us and the debenture trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series that is affected. However, unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, we and the debenture trustee may make the following changes only with the consent of each holder of any outstanding debt securities affected:

extending the fixed maturity of the series of debt securities;

reducing the principal amount, reducing the rate of or extending the time of payment of interest, or reducing any premium payable upon the redemption of any debt securities; or

reducing the percentage of debt securities, the holders of which are required to consent to any amendment, supplement, modification or waiver.

Discharge

Each indenture provides that we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for specified obligations, including obligations to:

register the transfer or exchange of debt securities of the series;

replace stolen, lost or mutilated debt securities of the series;

maintain paying agencies;

hold monies for payment in trust;

recover excess money held by the debenture trustee;

compensate and indemnify the debenture trustee; and

appoint any successor trustee.

In order to exercise our rights to be discharged, we must deposit with the debenture trustee money or government obligations sufficient to pay all the principal of, any premium, if any, and interest on, the debt securities of the series on the dates payments are due.

Table of Contents

Form, Exchange and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we provide otherwise in the applicable prospectus supplement, in denominations of $1,000 and any integral multiple thereof. The indentures provide that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company or another depositary named by us and identified in a prospectus supplement with respect to that series. See Legal Ownership of Securities for a further description of the terms relating to any book-entry securities.

At the option of the holder, subject to the terms of the indentures and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indentures and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange, we will impose no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

If we elect to redeem the debt securities of any series, we will not be required to:

- issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or

- register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Debenture Trustee

The debenture trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the debenture trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs. Subject to this provision, the debenture trustee is under no obligation to exercise any of the powers given it by the indentures at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, we will make interest payments by check that we will mail to the holder or by wire transfer to certain holders. Unless we otherwise indicate in the applicable prospectus supplement, we will designate the corporate trust office of the debenture trustee in the City of New York as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

13

Table of Contents

All money we pay to a paying agent or the debenture trustee for the payment of the principal of or any premium or interest on any debt securities that remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the debt security thereafter may look only to us for payment thereof.

Governing Law

The indentures and the debt securities will be governed by and construed in accordance with the laws of the State of New York, except to the extent that the Trust Indenture Act of 1939 is applicable.

Subordination of Subordinated Debt Securities

The subordinated debt securities will be unsecured and will be subordinate and junior in priority of payment to certain of our other indebtedness to the extent described in a prospectus supplement. The subordinated indenture does not limit the amount of subordinated debt securities that we may issue, nor does it limit us from issuing any other secured or unsecured debt.

DESCRIPTION OF WARRANTS

We may issue warrants for the purchase of common stock, preferred stock and/or debt securities in one or more series. We may issue warrants independently or together with common stock, preferred stock and/or debt securities, and the warrants may be attached to or separate from these securities. While the terms summarized below will apply generally to any warrants that we may offer, we will describe the particular terms of any series of warrants in more detail in the applicable prospectus supplement. The terms of any warrants offered under a prospectus supplement may differ from the terms described below.

We have filed forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants being offered as exhibits to the registration statement of which this prospectus is a part. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of warrant agreement, including a form of warrant certificate, that describes the terms of the particular series of warrants we are offering before the issuance of the related series of warrants. The following summaries of material provisions of the warrants and the warrant agreements are subject to, and qualified in their entirety by reference to, all the provisions of the warrant agreement and warrant certificate applicable to the particular series of warrants that we may offer under this prospectus. We urge you to read the applicable prospectus supplements related to the particular series of warrants that we may offer under this prospectus, as well as any related free writing prospectuses, and the complete warrant agreements and warrant certificates that contain the terms of the warrants.

General

We will describe in the applicable prospectus supplement the terms of the series of warrants being offered, including:

- the offering price and aggregate number of warrants offered;
- the currency for which the warrants may be purchased;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;
- if applicable, the date on and after which the warrants and the related securities will be separately transferable;
- in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at, and currency in which, this principal amount of debt securities may be purchased upon such exercise;
- in the case of warrants to purchase common stock or preferred stock, the number of shares of common stock or preferred stock, as the case may be, purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;

the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreements and the warrants;

the terms of any rights to redeem or call the warrants;

Table of Contents

any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;

the dates on which the right to exercise the warrants will commence and expire;

the manner in which the warrant agreements and warrants may be modified;

a discussion of any material or special United States federal income tax consequences of holding or exercising the warrants;

the terms of the securities issuable upon exercise of the warrants; and

any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

Before exercising their warrants, holders of warrants will not have any of the rights of holders of the securities purchasable upon such exercise, including:

in the case of warrants to purchase debt securities, the right to receive payments of principal of, or premium, if any, or interest on, the debt securities purchasable upon exercise or to enforce covenants in the applicable indenture; or

in the case of warrants to purchase common stock or preferred stock, the right to receive dividends, if any, or, payments upon our liquidation, dissolution or winding up or to exercise voting rights, if any.

Exercise of Warrants

Each warrant will entitle the holder to purchase the securities that we specify in the applicable prospectus supplement at the exercise price that we describe in the applicable prospectus supplement. Holders of the warrants may exercise the warrants at any time up to the specified time on the expiration date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

Holders of the warrants may exercise the warrants by delivering the warrant certificate representing the warrants to be exercised together with specified information, and paying the required amount to the warrant agent in immediately available funds, as provided in the applicable prospectus supplement. We will set forth on the reverse side of the warrant certificate and in the applicable prospectus supplement the information that the holder of the warrant will be required to deliver to the warrant agent.

Upon receipt of the required payment and the warrant certificate properly completed and duly executed at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement, we will issue and deliver the securities purchasable upon such exercise. If fewer than all of the warrants represented by the warrant certificate are exercised, then we will issue a new warrant certificate for the remaining amount of warrants. If we so indicate in the applicable prospectus supplement, holders of the warrants may surrender securities as all or part of the exercise price for warrants.

Governing Law

Unless we provide otherwise in the applicable prospectus supplement, the warrants and warrant agreements will be governed by and construed in accordance with the laws of the State of New York.

Enforceability of Rights by Holders of Warrants

Each warrant agent will act solely as our agent under the applicable warrant agreement and will not assume any obligation or relationship of agency or trust with any holder of any warrant. A single bank or trust company may act as warrant agent for more than one issue of warrants. A warrant agent will have no duty or responsibility in case of any default by us under the applicable warrant agreement or warrant, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a warrant may, without the consent of the related warrant agent or the holder of any other warrant, enforce by appropriate legal action its right to exercise, and receive the securities purchasable upon exercise of, its warrants.

DESCRIPTION OF UNITS

We may issue, in one more series, units consisting of common stock, preferred stock, debt securities and/or warrants for the purchase of common stock, preferred stock and/or debt securities in any combination. While the terms we have summarized below

Table of Contents

will apply generally to any units that we may offer under this prospectus, we will describe the particular terms of any series of units in more detail in the applicable prospectus supplement. The terms of any units offered under a prospectus supplement may differ from the terms described below.

We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of unit agreement that describes the terms of the series of units we are offering, and any supplemental agreements, before the issuance of the related series of units. The following summaries of material terms and provisions of the units are subject to, and qualified in their entirety by reference to, all the provisions of the unit agreement and any supplemental agreements applicable to a particular series of units. We urge you to read the applicable prospectus supplements related to the particular series of units that we may offer under this prospectus, as well as any related free writing prospectuses and the complete unit agreement and any supplemental agreements that contain the terms of the units.

General

Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date.

We will describe in the applicable prospectus supplement the terms of the series of units being offered, including:

- the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;
- any provisions of the governing unit agreement that differ from those described below; and
- any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units.

The provisions described in this section, as well as those described under Description of Capital Stock, Description of Debt Securities and Description of Warrants will apply to each unit and to any common stock, preferred stock, debt security or warrant included in each unit, respectively.

Issuance in Series

We may issue units in such amounts and in such numerous distinct series as we determine.

Enforceability of Rights by Holders of Units

Each unit agent will act solely as our agent under the applicable unit agreement and will not assume any obligation or relationship of agency or trust with any holder of any unit. A single bank or trust company may act as unit agent for more than one series of units. A unit agent will have no duty or responsibility in case of any default by us under the applicable unit agreement or unit, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a unit may, without the consent of the related unit agent or the holder of any other unit, enforce by appropriate legal action its rights as holder under any security included in the unit.

Title

We, and any unit agent and any of their agents, may treat the registered holder of any unit certificate as an absolute owner of the units evidenced by that certificate for any purpose and as the person entitled to exercise the rights attaching to the units so requested, despite any notice to the contrary. See Legal Ownership of Securities below.

LEGAL OWNERSHIP OF SECURITIES

We can issue securities in registered form or in the form of one or more global securities. We describe global securities in greater detail below. We refer to those persons who have securities registered in their own names on the books that we or any applicable

Table of Contents

trustee, depositary or warrant agent maintain for this purpose as the holders of those securities. These persons are the legal holders of the securities. We refer to those persons who, indirectly through others, own beneficial interests in securities that are not registered in their own names, as indirect holders of those securities. As we discuss below, indirect holders are not legal holders, and investors in securities issued in book-entry form or in street name will be indirect holders.

Book-Entry Holders

We may issue securities in book-entry form only, as we will specify in the applicable prospectus supplement. This means securities may be represented by one or more global securities registered in the name of a financial institution that holds them as depositary on behalf of other financial institutions that participate in the depositary s book-entry system. These participating institutions, which are referred to as participants, in turn, hold beneficial interests in the securities on behalf of themselves or their customers.

Only the person in whose name a security is registered is recognized as the holder of that security. Securities issued in global form will be registered in the name of the depositary or its participants. Consequently, for securities issued in global form, we will recognize only the depositary as the holder of the securities, and we will make all payments on the securities to the depositary. The depositary passes along the payments it receives to its participants, which in turn pass the payments along to their customers who are the beneficial owners. The depositary and its participants do so under agreements they have made with one another or with their customers; they are not obligated to do so under the terms of the securities.

As a result, investors in a book-entry security will not own securities directly. Instead, they will own beneficial interests in a global security, through a bank, broker or other financial institution that participates in the depositary s book-entry system or holds an interest through a participant. As long as the securities are issued in global form, investors will be indirect holders, and not holders, of the securities.

Street Name Holders

We may terminate a global security or issue securities in non-global form. In these cases, investors may choose to hold their securities in their own names or in street name. Securities held by an investor in street name would be registered in the name of a bank, broker or other financial institution that the investor chooses, and the investor would hold only a beneficial interest in those securities through an account he or she maintains at that institution.

For securities held in street name, we will recognize only the intermediary banks, brokers and other financial institutions in whose names the securities are registered as the holders of those securities, and we will make all payments on those securities to them. These institutions pass along the payments they receive to their customers who are the beneficial owners, but only because they agree to do so in their customer agreements or because they are legally required to do so. Investors who hold securities in street name will be indirect holders, not holders, of those securities.

Legal Holders

Our obligations, as well as the obligations of any applicable trustee and of any third parties employed by us or a trustee, run only to the legal holders of the securities. We do not have obligations to investors who hold beneficial interests in global securities, in street name or by any other indirect means. This will be the case whether an investor chooses to be an indirect holder of a security or has no choice because we are issuing the securities only in global form.

For example, once we make a payment or give a notice to the holder, we have no further responsibility for the payment or notice even if that holder is required, under agreements with depositary participants or customers or by law, to pass it along to the indirect holders but does not do so. Similarly, we may want to obtain the approval of the holders to amend an indenture, to relieve us of the consequences of a default or of our obligation to comply with a particular provision of the indenture or for other purposes. In such an event, we would seek approval only from the holders, and not the indirect holders, of the securities. Whether and how the holders contact the indirect holders is up to the holders.

Table of Contents

Special Considerations For Indirect Holders

If you hold securities through a bank, broker or other financial institution, either in book-entry form or in street name, you should check with your own institution to find out:

how it handles securities payments and notices;

whether it imposes fees or charges;

how it would handle a request for the holders consent, if ever required;

whether and how you can instruct it to send you securities registered in your own name so you can be a holder, if that is permitted in the future;

how it would exercise rights under the securities if there were a default or other event triggering the need for holders to act to protect their interests; and

if the securities are in book-entry form, how the depositary s rules and procedures will affect these matters.

Global Securities

A global security is a security that represents one or any other number of individual securities held by a depositary. Generally, all securities represented by the same global securities will have the same terms.

Each security issued in book-entry form will be represented by a global security that we deposit with and register in the name of a financial institution or its nominee that we select. The financial institution that we select for this purpose is called the depositary. Unless we specify otherwise in the applicable prospectus supplement, The Depository Trust Company, New York, New York, known as DTC, will be the depositary for all securities issued in book-entry form.

A global security may not be transferred to or registered in the name of anyone other than the depositary, its nominee or a successor depositary, unless special termination situations arise. We describe those situations below under Special Situations When a Global Security Will Be Terminated. As a result of these arrangements, the depositary, or its nominee, will be the sole registered owner and holder of all securities represented by a global security, and investors will be permitted to own only beneficial interests in a global security. Beneficial interests must be held by means of an account with a broker, bank or other financial institution that in turn has an account with the depositary or with another institution that does. Thus, an investor whose security is represented by a global security will not be a holder of the security, but only an indirect holder of a beneficial interest in the global security.

If the prospectus supplement for a particular security indicates that the security will be issued in global form only, then the security will be represented by a global security at all times unless and until the global security is terminated. If termination occurs, we may issue the securities through another book-entry clearing system or decide that the securities may no longer be held through any book-entry clearing system.

Special Considerations For Global Securities

The rights of an indirect holder relating to a global security will be governed by the account rules of the investor s financial institution and of the depositary, as well as general laws relating to securities transfers. We do not recognize an indirect holder as a holder of securities and instead deal only with the depositary that holds the global security.

If securities are issued only in the form of a global security, an investor should be aware of the following:

an investor cannot cause the securities to be registered in his or her name, and cannot obtain non-global certificates for his or her interest in the securities, except in the special situations we describe below;

an investor will be an indirect holder and must look to his or her own bank or broker for payments on the securities and protection of his or her legal rights relating to the securities, as we describe above;

an investor may not be able to sell interests in the securities to some insurance companies and to other institutions that are required by law to own their securities in non-book-entry form;

an investor may not be able to pledge his or her interest in a global security in circumstances where certificates representing the securities must be delivered to the lender or other beneficiary of the pledge in order for the pledge to be effective;

Table of Contents

the depositary s policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor s interest in a global security;

we and any applicable trustee have no responsibility for any aspect of the depositary s actions or for its records of ownership interests in a global security, nor do we or any applicable trustee supervise the depositary in any way;

the depositary may, and we understand that DTC will, require that those who purchase and sell interests in a global security within its book-entry system use immediately available funds, and your broker or bank may require you to do so as well; and

financial institutions that participate in the depositary s book-entry system, and through which an investor holds its interest in a global security, may also have their own policies affecting payments, notices and other matters relating to the securities.

There may be more than one financial intermediary in the chain of ownership for an investor. We do not monitor and are not responsible for the actions of any of those intermediaries.

Special Situations When a Global Security Will Be Terminated

In a few special situations described below, the global security will terminate and interests in it will be exchanged for physical certificates representing those interests. After that exchange, the choice of whether to hold securities directly or in street name will be up to the investor. Investors must consult their own banks or brokers to find out how to have their interests in securities transferred to their own name, so that they will be direct holders. We have described the rights of holders and street name investors above.

Unless we provide otherwise in the applicable prospectus supplement, the global security will terminate when the following special situations occur:

if the depositary notifies us that it is unwilling, unable or no longer qualified to continue as depositary for that global security and we do not appoint another institution to act as depositary within 90 days;

if we notify any applicable trustee that we wish to terminate that global security; or

if an event of default has occurred with regard to securities represented by that global security and has not been cured or waived.

The prospectus supplement may also list additional situations for terminating a global security that would apply only to the particular series of securities covered by the applicable prospectus supplement. When a global security terminates, the depositary, and not we or any applicable trustee, is responsible for deciding the names of the institutions that will be the initial direct holders.

PLAN OF DISTRIBUTION

We may sell the securities from time to time pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods. We may sell the securities to or through underwriters or dealers, through agents, or directly to one or more purchasers. We may distribute securities from time to time in one or more transactions:

at a fixed price or prices, which may be changed;

at market prices prevailing at the time of sale;

at prices related to such prevailing market prices; or

at negotiated prices.

A prospectus supplement or supplements will describe the terms of the offering of the securities, including:

the name or names of the underwriters, if any;

the purchase price of the securities and the proceeds we will receive from the sale;

any over-allotment options under which underwriters may purchase additional securities from us;

any agency fees or underwriting discounts and other items constituting agents or underwriters compensation;

Table of Contents

any public offering price;

any discounts or concessions allowed or reallowed or paid to dealers; and

any securities exchange or market on which the securities may be listed.

Only underwriters named in the prospectus supplement will be underwriters of the securities offered by the prospectus supplement.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to certain conditions, the underwriters will be obligated to purchase all of the securities offered by the prospectus supplement, other than securities covered by any over-allotment option. Any public offering price and any discounts or concessions allowed or reallowed or paid to dealers may change from time to time. We may use underwriters with whom we have a material relationship. We will describe in the prospectus supplement, naming the underwriter, the nature of any such relationship.

We may sell securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities and we will describe any commissions we will pay the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, our agent will act on a best-efforts basis for the period of its appointment.

We may authorize agents or underwriters to solicit offers by certain types of institutional investors to purchase securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in the prospectus supplement.

We may provide agents and underwriters with indemnification against civil liabilities, including liabilities under the Securities Act, or contribution with respect to payments that the agents or underwriters may make with respect to these liabilities. Agents and underwriters may engage in transactions with, or perform services for, us in the ordinary course of business.

All securities we may offer, other than common stock, will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities.

Any underwriter may engage in over-allotment, stabilizing transactions, short-covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Over-allotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum price. Syndicate-covering or other short-covering transactions involve purchases of the securities, either through exercise of the over-allotment option or in the open market after the distribution is completed, to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a stabilizing or covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

Any underwriters that are qualified market makers on the NASDAQ Global Market may engage in passive market making transactions in the common stock on the NASDAQ Global Market in accordance with Regulation M under the Exchange Act, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the common stock. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker s bid, however, the passive market maker s bid must then be lowered when certain purchase limits are exceeded. Passive

market making may stabilize the market price of the securities at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

In compliance with guidelines of the Financial Industry Regulatory Authority, or FINRA, the maximum consideration or discount to be received by any FINRA member or independent broker dealer may not exceed 8% of the aggregate amount of the securities offered pursuant to this prospectus and any applicable prospectus supplement.

Table of Contents

LEGAL MATTERS

The validity of the securities being offered by this prospectus will be passed upon by Cooley Godward Kronish LLP, Palo Alto, California.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2006, and management s assessment of the effectiveness of our internal control over financial reporting as of December 31, 2006, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements and management s assessment are incorporated by reference in reliance on Ernst & Young LLP s reports, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

We file annual, quarterly and special reports, proxy statements and other information with the SEC. You may read and copy any document we file at the SEC s Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference room. The SEC maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC, including GTx, Inc. The SEC s Internet site can be found at www.sec.gov.

The SEC allows us to incorporate by reference the information we file with it, which means that we can disclose important information to you by referring you to another document that we have filed separately with the SEC. You should read the information incorporated by reference because it is an important part of this prospectus. We incorporate by reference the following information or documents that we have filed with the SEC (Commission File No. 0-50549):

- our current report on Form 8-K filed with the SEC on February 26, 2007;
- our annual report on Form 10-K for the year ended December 31, 2006 filed with the SEC on March 9, 2007 (the 2006 10-K);
- the information specifically incorporated by reference into our 2006 Form 10-K from our definitive proxy statement on Schedule 14A filed with the SEC on March 14, 2007;
- our current report on Form 8-K filed with the SEC on April 17, 2007;
- our quarterly report on Form 10-Q for the quarter ended March 31, 2007 filed with the SEC on May 7, 2007;
- our current report on Form 8-K filed with the SEC on July 3, 2007;
- our current report on Form 8-K filed with the SEC on July 12, 2007;
- our current report on Form 8-K filed with the SEC on July 26, 2007;
- our current report on Form 10-Q for the quarter ended June 30, 2007 filed with the SEC on August 1, 2007;
- our current reports on Form 8-K filed with the SEC on November 6, 2007 (except for the information furnished under Item 2.02 or any related exhibit);
- our current report on Form 10-Q for the quarter ended September 30, 2007 filed with the SEC on November 9, 2007;
- our current report on Form 8-K filed with the SEC on December 13, 2007;

our current report on Form 8-K filed with the SEC on December 18, 2007; and

the description of our common stock, which is registered under Section 12 of the Exchange Act, in our registration statement on Form 8-A, filed with the SEC on January 13, 2004, including any amendments or reports filed for the purpose of updating such description.

Table of Contents

Any information in any of the foregoing documents will automatically be deemed to be modified or superseded to the extent that information in this prospectus or in a later filed document that is incorporated or deemed to be incorporated herein by reference modifies or replaces such information.

We also incorporate by reference any future filings (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items) made with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, until we file a post-effective amendment that indicates the termination of the offering of the securities made by this prospectus. Information in such future filings updates and supplements the information provided in this prospectus. Any statements in any such future filings will automatically be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

We will provide to each person, including any beneficial owner, to whom a prospectus is delivered, without charge upon written or oral request, a copy of any or all of the documents that are incorporated by reference into this prospectus but not delivered with the prospectus, including exhibits which are specifically incorporated by reference into such documents. Requests should be directed to: GTx, Inc., Attention: Corporate Secretary, 3 N. Dunlap Street, Van Vleet Building, Memphis, TN 38163, telephone (901) 523-9700.

Table of Contents

14,285,715 Shares
Common Stock

PROSPECTUS SUPPLEMENT

Sole Book-Running Manager
Lazard Capital Markets
October 27, 2010