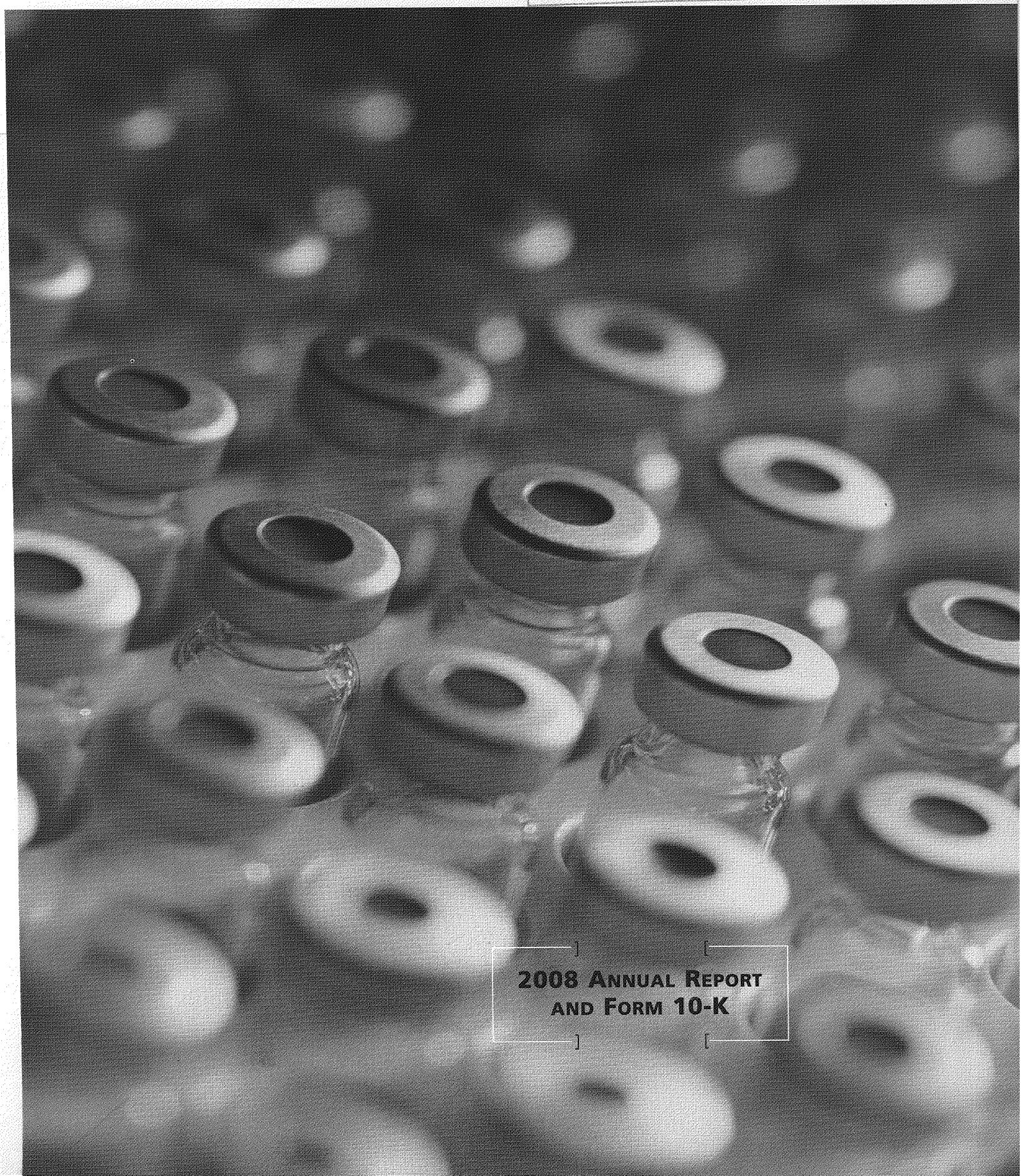
GTC Biotherapeutics, Inc.



2008 Annual Report and Form 10-K

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GTC Biotherapeutics

April 14, 2009

Dear Shareholders,

This past year has been a time of great progress for GTC culminating in early 2009 in the achievement of the most important milestone in the Company's history when the Food and Drug Administration approved ATryn®, our recombinant human antithrombin. For those of you who have been long term investors in GTC, you know that this has been a long journey. This is the first transgenically derived therapeutic protein ever approved by the FDA, and it has now been approved for use in both Europe and the United States. ATryn is also the only commercially available recombinant antithrombin in the world, and has been uniquely enabled by our transgenic technology. Being first is never easy. Our mammalian transgenic technology is the first new production technology approved for biologics in 20 years and is an accomplishment of which we are very proud. I would like to thank all the employees of GTC for this remarkable achievement.

The importance of this approval for GTC is very significant. In 2006 we achieved approval for ATryn in the European Union for use in antithrombin hereditary deficiency, or HD, patients undergoing surgery which at that time represented the first approval for a transgenically derived therapeutic protein anywhere in the world. That was a very important first. However, many investors and other observers, particularly in the USA, have always wanted to see the FDA approve ATryn and our production technology. The approval of ATryn for the prevention of thromboses in HD patients undergoing surgery or childbirth is, therefore, a landmark. At the same time that GTC received FDA approval, we also became the first company to receive approval under FDA's new genetic engineering regulations, known as GE, for transgenic animals, again a very major accomplishment.

With approval in the HD indication, we have now established a strong platform to expand the clinical development of ATryn into acquired deficiencies such as heparin resistance associated with coronary artery bypass surgery and disseminated intravascular coagulation (DIC) associated with severe sepsis, which represent major market opportunities that can be uniquely addressed by our

readily expandable supply of recombinant product. This is a clear advantage in a market that is inherently limited by the pool of donated blood available for plasma-derived products. There are a number of these potential acquired deficiency indications in which antithrombin is consumed as a result of a trauma. However, the approval of ATryn has a much greater significance, since this validation of our transgenic technology unlocks the value of the entire portfolio of products we have in development and establishes GTC as one of the small group of companies that have successfully developed a drug and received regulatory approval.

In the middle of 2008, we were very pleased to have entered into a licensing agreement with Ovation Pharmaceuticals for the commercialization and the further development of ATryn in the United States. Ovation has since been acquired by H. Lundbeck A/S of Denmark and is continuing as ATryn's US commercialization and development partner. Lundbeck began the process of launching ATryn as this letter went to press.

Lundbeck and GTC are also collaborating on a joint development plan for the potential use of ATryn in heparin resistant patients. Cardiac surgery involving use of a cardiopulmonary bypass machine, or CPB, requires that patients are anticoagulated prior to going on bypass, in order to avoid clot formation and other deleterious effects. Heparin is used to prevent the formation of blood clots. Heparin's ability to prevent clotting depends on the presence of sufficient antithrombin in the bloodstream to achieve the desired anticoagulant effect. It is estimated that over 20 percent of patients in CPB-related surgeries may exhibit heparin resistance. GTC has previously conducted studies related to this indication.

In Europe, we are in a period of transition from our former partner LEO Pharma which had been previously responsible for the commercialization and further development of ATryn in Europe, Canada and the Middle East. A number of potential partners have expressed interest in continuing this program in these same territories. We are developing a submission in Europe to expand the label for the approved indication to include childbirth in addition to surgical procedures. We are also preparing a submission for approval in the HD indication in Canada. Both of these regulatory filings will rely on the data we already obtained for our US and EU approvals. We also are engaged in discussions with potential partners for development of ATryn in Japan.

We have also continued to make significant progress in our other key programs:

- **Factor VIIa** - we have been developing a rabbit production system and in parallel have already established a commercial scale transgenic goat herd for recombinant human coagulation factor VIIa for the treatment of hemophilia under our joint venture agreement with LFB Biotechnologies of France. Together with LFB, we will make a decision regarding the animal of choice later this year. In either case, our plans are to enter the clinic early in 2010. Our transgenically produced Factor VIIa is expected to compete with Novo Nordisk's NovoSeven® which in 2008 had estimated sales of $1.3 billion dollars from approximately 1 kilogram of product. NovoSeven is a recombinant form of Factor VIIa for which the patents remain in force until 2011.

- **Factor IX** – is another coagulation factor for the treatment of hemophilia. GTC is developing this program using transgenic pigs as the production platform. This product is being developed in the LFB collaboration to compete with Wyeth's Factor IX product Benefix which had estimated sales of approximately $600 million in 2008. Our program is making progress according to plan and is running approximately 6 months behind Factor VIIa for entry into the clinic in 2010.

- **Alpha-1-Antitrypsin** is another recombinant plasma protein program in the LFB collaboration. Our process development activities have focused on technologies for extending the plasma half life of this product, and we have successfully identified alternatives for achieving this. We are discussing our clinical development plans for alpha-1 antitrypsin with the FDA with the goal of entering the clinic by early 2010.

- **Follow-on Biologics (FOBs)** - a key sector of our product portfolio in the future will be our monoclonal antibody programs, particularly FOB's. I believe GTC is very well positioned with our existing commercial scale production platform to develop a group of monoclonal antibodies as Follow-on Biologics for selected proprietary products that today have aggregate annual sales of over $17 billion. These products mostly come off patent over the next 5 – 6 years. Our focus is principally on large volume products which will be required to be produced in quantities of 100's of kilograms to be competitive. With the new administration committed to legislation enabling Follow-on Biologic approval and major companies beginning to declare their strategic interest in this area, I believe these programs will be important value drivers for GTC. We will be seeking partnering arrangements to support the development and commercialization of these products. We have initiated the development of the production systems for the first two of these programs and will be expanding the portfolio as partnering arrangements are established.

In addition, we have entered into a collaboration with New Zealand's AgResearch NZ, including a grant from the New Zealand government, to develop Follow-on Biologics which can take advantage of different patent timelines outside the United States. Since its early days, GTC has maintained a reserve herd of non-transgenic goats in New Zealand and our existing herd was originally sourced from New Zealand, which has a unique record in the world for the health of its animals. The science and development capabilities in New Zealand are very strong, and we believe this collaboration will make an important addition to our strategy for Follow-on Biologics in both expanding our capabilities and shortening our time to market.

- **CD20** - as we have reported previously, we have goats producing a CD20 monoclonal antibody, which is a molecule brought into our collaboration by LFB. This is not an identical molecule to Genentech's Rituxan® which is being currently used to treat non-Hodgkins lymphoma, but it binds to the same target. The initial analysis of this molecule produced in our transgenic system indicates that the significantly enhanced antibody dependent cell cytotoxicity (ADCC) over Rituxan which we had predicted based on the natural low fucose levels from the goat mammary system. This is shaping up as an exciting program, and we are seeking a commercial partner to support our development of this product in North America.

We have entered into a collaboration and licensing agreement with JCom Ltd. in S. Korea, which is closely affiliated with Dong-A, a leading pharmaceutical company in Korea, for the development of a transgenic production system for their recombinant insulin products. Our agreement includes payments to us for work we perform, as well as success payments and future royalties. This agreement broadens our opportunities for successful work in an externally partnered product.

We have also continued our collaboration with PharmAthene for their Protexia® product, and we will continue to seek collaborations where there is a clear commitment to our production system to ensure we build long term value.

Our progress with these programs is vital to our partnering strategy both for proprietary products and external contracts and service agreements, and we believe that these partnerships will make an important contribution to our financial well being.

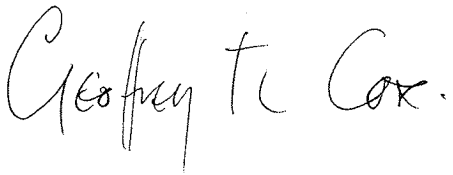
During the latter part of 2008, GTC completed an agreement with LFB Biotechnologies for a $15 million financing in which GTC issued convertible debt and warrants to purchase shares of GTCB common stock on the terms previously disclosed. The net proceeds at closing, after transaction costs and establishment of a restricted cash account, were approximately $10 million. As this letter goes to press, we are working on additional options to strengthen our balance sheet.

I believe the FDA approval of ATryn is a remarkable achievement and will provide the foundation on which we can proceed with confidence to build a significant company. There is no doubt that it changes substantially the perspective of the opportunities which can be achieved with ATryn and our portfolio of products in recombinant plasma proteins and Follow-on Biologics.

We look forward to 2009, and do so with optimism and with the belief that we can successfully meet the challenges of our industry and play an important role in the future production and commercialization of therapeutic proteins using our unique production technology. I wish to thank all of our investors for their continued support of GTC throughout the year. 2009 should prove to be a very exciting year as we continue to transform and focus the company towards commercialization.

I invite you to learn more about us in our enclosed Annual Report on Form 10-K filed with the Securities and Exchange Commission. I also encourage you to keep current on our developments by periodically checking our web site, www.gtc-bio.com. I look forward to updating you on our progress over the coming months.

Sincerely,



Geoffrey F. Cox, Ph.D.
Chairman of the Board and Chief Executive Officer

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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 28, 2008

or

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

For the transition period from _____ to _____

Commission File No. 0-21794

GTC BIOTHERAPEUTICS, INC.

(Exact name of Registrant as Specified in Its Charter)

MASSACHUSETTS	**04-3186494**
(State or Other Jurisdiction of Incorporation or Organization)	*(I.R.S. Employer Identification No.)*
175 CROSSING BOULEVARD FRAMINGHAM, MASSACHUSETTS	**01702**
(Address of Principal Executive Offices)	*(Zip Code)*

(508) 620-9700
(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

Common Stock, par value $0.01 per share Rights to Purchase Series C Junior Participating Cumulative Preferred Stock	**Nasdaq Capital Market**
Title of each class	**Name of each exchange on which registered**

Securities registered pursuant to Section 12(g) of the Act:

None

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒

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

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

Indicate by check mark whether the Registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer or a smaller reporting company. See the definitions of "accelerated filer, large accelerated filer and smaller reporting company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer ☐ Accelerated filer ☐ Non-accelerated filer ☒ Smaller reporting company ☐

Indicate by check mark whether the Registrant is a shell company (as defined by Rule 12b-2 of the Act). Yes ☐ No ☒

The aggregate market value of voting and non-voting common stock held by non-affiliates of the Registrant as of June 29, 2008, the last business day of the registrant's most recently completed second fiscal quarter, was approximately $37,732,462, based on the closing sale price of the registrant's Common Stock as reported on the Nasdaq Global Market.

Number of shares of the registrant's Common Stock outstanding as of February 20, 2009: 104,315,898

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's Proxy Statement for the Annual Meeting of Stockholders scheduled to be held May 22, 2009 are incorporated by reference into Part III of this Form 10-K.

GTC Biotherapeutics, Inc.
Form 10-K
For the Fiscal Year Ended December 28, 2008
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PART I

In this Annual Report on Form 10-K, or Annual Report, the words "we", "our", "ours" and "us" refer only to GTC Biotherapeutics, Inc., its wholly-owned subsidiaries and its joint venture. Unless indicated otherwise, references to the years 2008, 2007 and 2006 refer to our fiscal years ended December 28, 2008, December 30, 2007 and December 31, 2006, respectively.

NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report contains forward-looking statements, including statements regarding future revenues, research and development programs, clinical trials and collaborations and our future cash requirements. The words or phrases "will", "will likely result", "are expected to", "will continue", "is anticipated", "estimate", "project", "potential", "believe", "plan", "anticipate", "expect", "intend", or similar expressions and variations of

such words are intended to identify forward-looking statements. Statements that are not historical facts are based on our current expectations, beliefs, assumptions, estimates, forecasts and projections for our business and the industry and markets related to our business. The statements contained in this report are not guarantees of future performance and involve certain risks, uncertainties and assumptions which are difficult to predict. Therefore, actual outcomes and results may differ materially from what is expressed in such forward-looking statements. Important factors which may affect future revenues, research and development programs, clinical trials and collaborations and our future cash requirements include, without limitation, continued operating losses, our ability to raise additional capital, technology risks to our transgenically produced products, the performance of our collaboration partners and continuation of our collaborations, our ability to enter into collaborations in the future and the terms of such collaborations, regulatory approval of our transgenically produced products, preclinical and clinical testing of our transgenically produced products, and those factors set forth in the Section entitled "Risk Factors" in Item 1A of this Form 10-K.

ITEM 1. BUSINESS

Overview

We are the leader in the development and production of human therapeutic proteins through transgenic technology that enables animals to produce what is known as a recombinant form of a specified human protein in their milk. Using this technology, we are developing a portfolio of recombinant blood proteins to treat a range of genetic and acquired blood deficiencies, including hemophilia and other blood coagulation disorders. These blood proteins, also known as plasma proteins, are difficult to produce in other manufacturing systems, and some are currently only available by extraction from human blood. We have also initiated the development of a portfolio of monoclonal antibodies, or MAbs, for use as potential follow-on biologics targeted at several large market products. We also continue to provide services for external partners as a continuing source of cash and revenue.

Our first product, ATryn®, is a recombinant form of human antithrombin, a blood protein with anticoagulation and anti-inflammatory properties. In 2006, ATryn® became the first transgenically produced therapeutic protein to be approved anywhere in the world when we obtained the European Commission's approval of the use of ATryn® as a prophylactic treatment for patients with hereditary antithrombin deficiency, or HD, undergoing surgical procedures. On February 6, 2009, we received United States Food and Drug Administration, or FDA, approval for ATryn® for HD patients undergoing surgery or childbirth in the United States, making ATryn® the first transgenically derived therapeutic protein approved by the FDA. The FDA has also designated ATryn® an Orphan Drug in this indication. Along with the approval of ATryn®, the FDA's Center for Veterinary Medicine also approved our New Animal Drug Application, the first of its kind to regulate genetically engineered animals. This is now required for a recombinant technology used to develop transgenic animals, such as the goats that produce recombinant antithrombin. We believe that the regulatory approval of ATryn® in Europe and the U.S. achieved an important validation of our production technology which will assist in obtaining approvals for other compounds and in other countries.

We plan to develop our portfolio of recombinant proteins through strategic collaborations:

- In June 2008, we entered into a collaboration agreement with OVATION Pharmaceuticals to develop and market ATryn® in the United States. The collaboration agreement includes the commercialization of ATryn® in the HD indication and the further development of ATryn® in acquired antithrombin deficiency indications, or AD.
- In September 2006, we entered into a collaboration agreement with LFB Biotechnologies, or LFB, to develop selected recombinant plasma proteins and MAbs. The first program in this collaboration is for the development of a recombinant form of human blood coagulation factor VIIa for the treatment of patients with hemophilia. This collaboration has now been established in a separate joint venture entity, and we have added to the joint venture programs to develop a recombinant form of human blood coagulation factor IX, recombinant human alpha-1 antitrypsin, as well as an antibody to the CD20 immune system receptor, the same target as for the MAb marketed as Rituxan®.

The following summarizes our portfolio of proprietary products in development:

Recombinant Plasma Protein Products

We believe that our transgenic technology offers well-characterized supplies of recombinant forms of therapeutic human plasma proteins. Therapeutic human plasma proteins have traditionally been derived from the plasma portion of human blood but in some cases have also been produced using recombinant DNA techniques. The availability of plasma-derived proteins is limited by the capabilities of the blood collection system. Many plasma proteins are difficult to express in economically viable quantities in traditional recombinant production technologies such as mammalian cell culture or bacteria production. We believe that our transgenic recombinant production technology offers:

- A greater capability to produce difficult-to-express recombinant plasma proteins in large quantities in a cost effective manner;
- the ability to expand the current markets for existing indications that are constrained by low production quantities and high production costs and prices;
- the ability to establish new or expanded markets based on the development of new indications and a greater supply of these therapeutic proteins; and
- the ability to develop transgenic animals and maintain appropriate production facilities with substantially lower capital investment than building a cell culture bioreactor production facility.

Our estimation of the potential market for recombinant forms of plasma proteins is based, in part, on the sales experience of recombinant forms of the blood coagulation proteins known as factors VIIa, VIII, and IX, which have generated $5 billion of annual sales worldwide compared to the $1.1 billion of annual sales worldwide for plasma-derived coagulation factor products. These recombinant products have been developed for multiple indications which have expanded their markets. By increasing the number of approved indications for our proprietary recombinant plasma proteins, we believe we have the opportunity for similar success in expanded markets.

- **ATryn®:** Our first product, ATryn®, is approved in the U.S. for the treatment of HD patients undergoing surgery or childbirth. The FDA has designated ATryn® an Orphan Drug, providing seven years of market exclusivity in this indication. OVATION, our partner for ATryn® in the U.S., is planning for commercial launch in the second quarter of 2009. While the initial HD indication is expected to be a modest market, our collaboration with OVATION provides for the further clinical development of ATryn® for larger AD indications in the U.S. The first of these indications is expected to be heparin resistance in cardiopulmonary bypass surgery where we believe our existing clinical data in this indication will allow us to proceed to a Phase III study. We estimate the market opportunity for the heparin resistance indication in the U.S. is approximately $100 million to $150 million. We estimate that the existing worldwide annual sales for plasma-sourced antithrombin is approximately $250 million, split principally between Japan and Europe, with $12 - $15 million being sold in the U.S. as Thrombate III® by Talecris. Historically there has been limited availability of plasma-derived antithrombin in the U.S., and this product has not been developed in the broader AD indications. Antithrombin products from European-sourced plasma cannot be sold in the U.S.

  We also have a collaboration agreement with LEO Pharma A/S, or LEO, for the commercialization of ATryn® in HD in Europe, Canada, and the Middle East and for its further development in AD indications. LEO selected disseminated intravascular coagulation associated with severe sepsis, or DIC, as the first AD indication in which to conduct additional clinical studies under this collaboration. In the third quarter of 2008, LEO advised us that, as a result of an internal re-assessment of their strategic priorities, they wished to enter in to negotiations to transfer the ATryn® program to us or an alternate partner. Pending any such transfer, further patients are not being enrolled in the study at this time. LEO has made it clear that their decision was not based on any safety or efficacy issues. We are currently engaged in a dispute resolution process with LEO, as described under Item 3 in this Annual Report. We estimate that the annual market opportunity for DIC in the U.S. alone is $2 - 3 billion.

- **rhFVIIa:** We are developing a recombinant human coagulation factor VIIa, or rhFVIIa, a blood protein for the treatment of hemophilia, as the first program in our joint venture with LFB. We have begun developing the production system for rhFVIIa, and we anticipate initiating clinical studies in 2010 to evaluate our rhFVIIa in treating hemophiliacs who have developed inhibitors to coagulation factors VIII or IX. An existing rhFVIIa product, marketed as NovoSeven® by Novo Nordisk, is commercially available today at a selling price of approximately $1,000/mg. The patents for NovoSeven® expire in 2011. The estimated 2008 annual sales of NovoSeven® were $1.2 billion. We believe our rhFVIIa product will cost less to produce and offer attractive profit margins at a lower selling price, which in turn may expand patient usage and broaden geographic distribution.
- **rhFIX:** In late 2007, we obtained a license from ProGenetics, LLC, granting us exclusive rights in North America, Europe and Japan to commercially develop recombinant human factor IX, or rhFIX, a blood coagulation factor for the treatment of type B hemophilia. An existing rhFIX product marketed as BeneFIX® by Wyeth is commercially available with estimated 2008 annual sales of $587 million. One estimate projects that the total annual market size for BeneFIX® could be $1 billion within the next four years. In 2008 this program was brought into our joint venture with LFB. ProGenetics is responsible for the production of rhFIX in the milk of transgenic pigs. We are responsible for developing the downstream processing, conducting clinical programs and managing regulatory requirements. We anticipate initiating clinical studies for rhFIX in 2010. As with rhFVIIa, we believe our product will cost less to produce and offer attractive profit margins at a lower selling price.
- **rhAAT:** We have developed goats that produce a recombinant form of human alpha-1 antitrypsin, or rhAAT, an inhibitor of elastase. Scientists believe that uninhibited elastase activity in the lungs may be the cause of emphysema and several other respiratory disorders, including chronic obstructive pulmonary disease. Patients with hereditary deficiency of alpha-1 antitrypsin are likely to experience declining lung function throughout their lives. The genetic defect leading to hereditary deficiency is estimated to exist in over 3 million people worldwide, although the deficiency is significantly under-diagnosed and under-treated. If shown to be safe and efficacious, successful treatment will require chronic dosing. In 2008, this program was also brought into our joint venture with LFB. Currently the U.S. market for plasma-derived alpha-1 antitrypsin is approximately $400 million and is dominated by Prolastin® produced by Talecris. We anticipate initiating clinical studies for rhAAT in 2010.

Follow-on Biologics

We believe production of monoclonal antibodies, or MAbs, using our transgenic production technology has economic advantages in large scale production compared to mammalian cell culture, including significantly lower capital investment and lower cost of goods. We are targeting several therapeutic MAbs which in total had worldwide sales of more than $17 billion in 2008. The patents for the first generation of these therapeutic MAbs begin to expire in 2013, creating a significant opportunity for companies that are capable of producing biosimilar versions of the innovator products, which are also known as follow-on biologics. This market opportunity combines relatively low risk with high returns from sales in large, established markets. Legislation to enable the approval of follow-on biologics by the FDA is currently under consideration by Congress. Our plan is to develop a portfolio of four to five MAbs as potential follow-on biologics which have patents expiring from 2013 onwards. We have initiated the development of the production systems for two of these programs. We are seeking partnerships to support the development and commercialization of our portfolio of follow-on MAbs. We also have a development agreement in place with AgResearch in New Zealand for the co-funding of further development of selected follow-on biologics.

- **CD20 MAb:** Under our joint venture with LFB, we are developing a MAb to the CD20 immune system receptor, which is expected to have target specificity similar to Rituximab® (Rituxan®, Mabthera®). This antibody is anticipated to have a relatively higher Antibody Dependent Cell-mediated Cytotoxicity, or ADCC, than Rituximab®. ADCC is the measure by which antibodies bind to target cells, making them more vulnerable to attack by immune cells. Rituximab® is used as a single-agent treatment for relapsed or refractory indolent Non-Hodgkin Lymphoma, or NHL, and also in

combination with chemotherapy for the treatment of aggressive NHL. Rituximab® has also received marketing approval in both the EU and the U.S. for rheumatoid arthritis. Sales of Rituximab® were $5 billion in 2008. It is unclear whether this program, if successfully developed, will be classified as a follow-on biologic until final legislation and regulations are established.

External Programs

In addition to our proprietary programs, we have programs in which our collaboration partner owns the underlying product rights while we are contracted to produce or purify the product through our transgenic technology. We refer to these as our external programs.

- **PharmAthene, Inc.:** We have provided PharmAthene, Inc. a license to our broad patent for the production of Protexia® in transgenic goats. Protexia® is a recombinant form of butyrylcholinesterase that is being developed by PharmAthene as a pre- and post-exposure therapy for casualties on the battlefield or civilian victims of nerve agent attacks. We are developing the downstream manufacturing and purification process under a development contract for this product. We are also manufacturing product for preclinical and clinical studies. PharmAthene's development of Protexia® as a biodefense product is funded by the United States Department of Defense, or DOD.
- **JCOM:** In February 2009, we entered into a licenses and development agreement with JCOM Co. Ltd., a subsidiary of Dong-A Pharmaceuticals, whereby we granted to JCOM an option for an exclusive license for Asia and a separate option for a co-exclusive license for the rest of the world, under our patent and know-how rights to make, use, sell, offer for sale and import recombinant human insulin products in these territories. Over the next 12 months, we plan to develop appropriate cell lines and demonstrate production of recombinant human insulin products for JCOM. The agreement contemplates the subsequent establishment of a transgenic production system in South Korea.

Partnering Strategy

Until our product revenues grow large enough to result in positive operating cash flow, we are primarily dependent upon funding from equity financings, partnering programs and proceeds from short and long-term debt to finance our operations. With regulatory validation of our production technology in the U.S. and Europe and our broad patent in the U.S. for transgenic production in animal milk, our strategy is to expand our partnering arrangements across the range of our portfolio of products.

Proprietary Product Programs

The level and speed of development of our proprietary products will be dependent upon our financial resources and new partnering arrangements as well as progress made in the legislative process in the U.S. as related to follow-on biologics. Our proprietary product programs are listed below in order of their priority.

ATryn® (Recombinant Human Antithrombin)

Antithrombin is a protein found in the plasma of human blood that has anticoagulant and anti-inflammatory properties. Antithrombin, as is typical of many plasma proteins, is difficult to express in commercially viable quantities using traditional recombinant production methods. Scientists estimate that approximately 1 in 2,000 to 5,000 people have HD, which suggests that approximately 60,000 to 150,000 people in the U.S. have HD.

Patients with HD have low levels of antithrombin in their blood stream and are prone to spontaneously develop thromboses from puberty onwards. Once patients are aware that they have this disorder, they can normally be treated prophylactically with blood thinners such as warfarin or Coumadin®. When these HD patients are undergoing high risk procedures, such as surgery or childbirth, the preferred course of treatment is to take them off their blood thinners and give them antithrombin to bring their antithrombin to normal levels in order to prevent the occurrence of thromboembolisms during the course of such procedures. The use of antithrombin in this indication, therefore, is an acute treatment for a chronic disorder.

We have developed a transgenically produced recombinant form of antithrombin, known as ATryn®. ATryn® has been approved in the U.S. for patients undergoing surgery or childbirth and in the EU for patients undergoing surgical procedures. Our intention is to file for label expansion in the EU for patients undergoing childbirth. As part of the FDA approval we are required to conduct a post-marketing surveillance study to continue gathering data on this rare patient population.

Our strategy is to leverage the availability of ATryn® with readily scalable production capacity to support the development of additional clinical indications and the creation of markets significantly in excess of those supported by today's plasma-sourced products. We also plan to seek approval for AD indications in the U.S. and Europe, and to develop ATryn® in Japan and the rest of the world through further partnering arrangements.

We estimate that the existing worldwide annual sales for plasma-sourced antithrombin is approximately $250 million, split principally between Japan and Europe, with $12 - $15 million being sold in the U.S. as Thrombate III® by Talecris. Historically there has been limited availability of plasma-derived antithrombin in the U.S., and this product has not been developed in the broader AD indications. Antithrombin products from European-sourced plasma cannot be sold in the U.S.

We have a collaboration agreement with OVATION to develop and market ATryn® in the United States. The collaboration agreement includes the commercialization of ATryn® in the HD indication and the further development of ATryn® in AD indications. The milestone payments to us under this agreement include a total of $9 million through approval of ATryn® for HD in the U.S. The collaboration anticipates further development of ATryn® in larger market acquired deficiencies such as the treatment of heparin resistance in patients undergoing cardiopulmonary bypass surgery and the treatment of DIC associated with severe sepsis, or DIC. These deficiencies result when a medical condition leads to consumption or loss of native antithrombin in a patient's bloodstream at a rate significantly in excess of the body's ability to replace it. The AD indications may lead to subsequent complications that increase patient risk for morbidity and mortality. Other examples of AD conditions include severe burns and bone marrow transplant procedures.

Under our agreement with OVATION, we are planning to develop ATryn® for the treatment of heparin resistance in patients undergoing coronary artery bypass graft (CABG) surgery that requires the use of a cardio pulmonary bypass (CPB) machine. Patients undergoing this surgery require anticoagulation with heparin to prevent clotting, which can occur when blood comes into contact with the tubing of the CPB machine performing the heart's function during surgery. Patients with heparin resistance generally do not respond adequately to the dose of heparin normally required to achieve sufficient anticoagulation for them to go on to the CPB machine. The overall incidence of heparin resistance has been reported to range from 10% to over 22% of CABG patients. Treatment of heparin resistant patients with fresh frozen plasma, which contains low concentrations of antithrombin, is one option to restore heparin sensitivity and achieve adequate anticoagulation to permit initiation of CPB. We previously completed two studies in the heparin resistance indication, and we are planning to conduct one additional Phase III study to determine the safety and efficacy of ATryn® in restoring heparin sensitivity in heparin resistant CABG patients as a basis for marketing approval in this indication.

Under our OVATION collaboration, we are responsible for production of ATryn® and will receive a transfer price, including a margin, for commercial product, a royalty on net sales, $257 million in potential clinical, regulatory and sales milestone payments, including those already received, and payment for product used in clinical trials. Our agreement provides for OVATION to further develop ATryn® in AD and fund our anticipated costs of clinical development. OVATION will be responsible for sales and marketing of ATryn® in the U.S., including all launch activities, which are scheduled to commence in the second quarter of 2009.

We also have a collaboration agreement with LEO Pharma A/S, or LEO, for the commercialization of ATryn® in HD in Europe, Canada, and the Middle East and for its further development in AD indications. LEO selected DIC associated with severe sepsis as the first AD indication in which to conduct additional clinical studies under this collaboration. In DIC, the septic infection consumes the patient's native antithrombin faster than the body can replace it, leading to clotting and inflammation problems that can cause death. Of the approximately

220,000 patients in the European Union and 250,000 patients in the U.S. with DIC in severe sepsis annually, approximately 50% die from the condition. We estimate that the annual market potential for DIC in the U.S. alone is $2 - 3 billion.

LEO initiated a Phase II dose-ranging study in the DIC indication in 2007. In the third quarter of 2008, LEO advised us that, as a result of an internal re-assessment of their strategic priorities, they wished to enter into negotiations to transfer the ATryn® program to us or an alternate partner. Pending any such transfer, further patients are not being enrolled in the study at this time. LEO has made it clear to us that their decision was not based on any safety or efficacy issues. We are currently engaged in a dispute resolution process with LEO, as described under Item 3 in this Annual Report.

Recombinant Factor VIIa (rhFVIIa)

We are developing rhFVIIa as the first program under our joint venture with LFB to develop recombinant human plasma proteins and MAbs. Factor VIIa is used in treating Type A and Type B hemophilia patients who have developed inhibitors to other blood coagulation products. Type A hemophilia is a genetic deficiency in the production of factor VIII. Type B hemophilia is a genetic deficiency in the production of factor IX. Both factors VIII and IX are involved in the body's ability to produce blood clots. A deficiency in either factor can prevent normal blood coagulation, resulting in abnormal and spontaneous bleeding. Patients develop inhibitors when their immune system incorrectly recognizes supplemental factors VIII or IX as foreign and generates antibodies to impede them. Providing supplemental factor VIIa, which is already present in blood, reduces the likelihood of initiating an immune response and enables the formation of blood clots even with the existing factor VIII or IX deficiency. This is the indication that is anticipated to be developed initially. There are also potential indications of excessive bleeding where a factor VIIa product may have therapeutic value in establishing an effective blood clot.

Novo Nordisk, which sells a recombinant factor VIIa, has disclosed that sales of NovoSeven® were $1.2 billion for 2008 from about 1kg of material, or approximately $1,000/mg. Our transgenic production technology can produce essentially unlimited quantities, which may support the pricing of our rhFVIIa at levels which would enable its utilization in a broader range of indications and geographical territories.

The research program for rhFVIIa was initiated by LFB and became the first program in our LFB collaboration in 2007. We have now developed transgenic production of rhFVIIa. We plan to initiate clinical development of rhFVIIa in 2010.

Recombinant Factor IX (rhFIX)

In late 2007, we obtained a license from ProGenetics, LLC, granting us exclusive rights in North America, Europe and Japan for commercial development of recombinant human factor IX, or rhFIX, a blood coagulation factor for the treatment of type B hemophilia. ProGenetics is responsible for the production of rhFIX in the milk of its existing herd of transgenic pigs. We are responsible for developing the downstream processing, conducting clinical programs and managing regulatory requirements. This program is now being developed as part of our joint venture with LFB. We also obtained exclusive rights from ProGenetics to develop recombinant human factor VIII, a blood coagulation factor for the treatment of type A hemophilia, as well as fibrinogen, a component of blood clots. We are not yet developing this recombinant human factor VIII. We have subsequently licensed the exclusive license to the transgenic production of fibrinogen to Pharming N.V.

We plan to initiate clinical development of rhFIX in 2010.

Recombinant Alpha-1 Antitrypsin (rhAAT)

Alpha-1 antitrypsin, AAT, is a blood protein that is known to be an inhibitor of elastase. Scientists believe that uninhibited elastase activity in the lungs may lead to the progressive development of emphysema and several other respiratory disorders, including chronic obstructive pulmonary disease, severe asthma and cystic fibrosis. Patients diagnosed with AAT deficiency can be treated weekly with injections of AAT to mitigate the onset of

these debilitating conditions. Like antithrombin, AAT is a product that is currently sourced from fractionated human plasma and has proven difficult to express in traditional recombinant production systems in economically viable quantities.

We have begun development of a recombinant form of AAT, or rhAAT. We believe that we can provide a highly pure and unconstrained supply of rhAAT to the market using goats we have developed that produce it in significant quantities. Our plan is to reach an understanding about the clinical development requirements for rhAAT with the FDA and to initiate clinical studies in 2010. In 2008, this program was brought into our joint venture with LFB. Our objective is to establish partnership arrangements to support our contributions to the further development and commercialization of rhAAT in the U.S.

We estimate that plasma-sourced AAT products currently generate worldwide annual sales of between $300 million to $400 million, principally in the U.S. The largest supplier of plasma-derived AAT in the U.S. is Talecris. Talecris has disclosed that sales of its Prolastin® product were $277 million in 2007. Similar to our other recombinant plasma protein programs, we believe the market for our rhAAT product may be expanded significantly beyond the market for the current plasma-derived products as a result of our unconstrained production capacity. This is an hereditary condition which is significantly under-diagnosed and under-treated. We also see further opportunities for multiple indications, which we believe will require the development of pulmonary delivery systems.

Follow-on Biologics or Biosimilars

We believe that the cost and large scale supply advantages of our transgenic production technology are ideally suited to developing cost-effective, follow-on biologics, particularly MAbs, once the innovator biologics no longer have patent protection. MAbs are proteins that are generated by the immune system and bind to a specific target. MAbs typically express at reasonable levels in traditional recombinant production systems, but are often required in large quantities for their use in chronic disease indications. The patents for the first generation of therapeutic MAbs and other antibody-like proteins begin to expire in 2013, creating a significant opportunity for companies that are capable of producing biosimilar versions of the innovator products. The regulatory path for biosimilar products following patent expiration has been defined in Europe, and the U.S. Congress is considering similar legislation. We anticipate that each follow-on product will generally require some level of clinical study, although not necessarily as extensive as that performed for the innovator antibody. We also have a development agreement in place with AgResearch in New Zealand for co-funding further development of selected follow-on biologics.

We have demonstrated transgenic production of a number of MAbs in both our proprietary and contract research and development programs. We have several patents covering the production of MAbs in the milk of transgenic mammals, along with other transgenic process patents, which we believe establish a strong proprietary position in the field. This intellectual property position enables development and commercial production of MAbs without relying on patents normally associated with cell culture and bacterial production technologies.

The level and speed of development of follow-on biologics will be dependent upon our financial resources and new partnering arrangements, as well as progress made in the legislative process.

CD20 Monoclonal Antibody (MAb)

Under our joint venture with LFB, we are developing a MAb to the CD20 immune system receptor, which is expected to have target specificity similar to Rituximab® (Rituxan®, Mabthera®). The existing relevant CD20 MAb patents will expire by 2014. However, this CD20 MAb is not identical to Rituximab®, and it may possess advantageous characteristics such as enhanced ADCC, which results in antibodies binding to target cells, making them more vulnerable to attack by immune cells. Once the legislation for follow-on biologics has been established we will be able to better assess the potential for developing this product as a follow-on biologic. Rituximab® is used in the treatment of B-cell non-Hodgkin's lymphoma, B-cell leukemia and rheumatoid arthritis. It is also under investigation for a range of other autoimmune conditions. Rituximab® had worldwide sales of $5 billion in 2008.

Other Programs

CD137 Antibody

We have developed animals that produce an antibody to CD137, also known as 4-1BB receptor, which is present on T-cells of the human immune system as well as some cancer cells. Our CD137 antibody may have therapeutic value primarily through the modulation of the immune system. As a result, we believe it has potential for use in multiple clinical applications, including cancer and autoimmune diseases. We anticipate that the potential quantities of our CD137 antibody required for future treatment could be very large. We believe that the increase in production capacity necessary to merit this anticipated demand for a CD137 antibody can be achieved more economically by using our transgenic production technology rather than traditional cell culture and bacteria production methods.

We have obtained key patent rights to the CD137 antibody from the Mayo Clinic. These rights extend to any patents issued under its patent applications. The level and speed of development of a CD137 antibody product will be dependent upon our financial resources and our ability to partner this program.

External Programs

Our external programs are ones in which the partner owns the underlying product rights. We believe that the advantages to an external partner of using our transgenic production technology include enabling the development of proteins that are difficult to produce in traditional recombinant production systems, requiring significantly lower capital investment, assuring lower cost of goods, and providing for flexibility in production capacity expansion. To date, we have had a number of external programs where we have successfully developed a transgenically produced version of the partner's protein on a service contract basis.

We currently have the following external programs:

PharmAthene, Inc.

We entered into a license and services agreement with PharmAthene, Inc. for their Protexia® product. Protexia® is a recombinant form of human butyrylcholinesterase produced by PharmAthene in the milk of their transgenic goats. PharmAthene is developing Protexia® as a pre- and post-exposure therapy for military or civilian victims of a chemical nerve agent attack. The development of Protexia® is funded by the Department of Defense. The agreement includes rights to utilize our transgenic technology in the worldwide development and commercialization of Protexia® for all uses. We have provided PharmAthene clinical supply and manufacturing services for Protexia®.

JCOM Co. Ltd.

In February 2009, we entered into a licenses and development agreement with JCOM Co. Ltd., a subsidiary of Dong-A Pharmaceuticals, whereby we granted to JCOM an option for an exclusive license for Asia and, a separate option for a co-exclusive license for the rest of the world, under our patent and know-how rights to make, use, sell, offer for sale and import recombinant human insulin products in these territories. Over the next 12 months we plan to develop appropriate cell lines and demonstrate production of recombinant human insulin products for JCOM. The agreement contemplates the subsequent establishment of a transgenic production system in South Korea.

Transgenic Production Technology

Overview

Applying our transgenic production technology, we insert human protein-specific DNA into the genetic structure of an animal to enable it to produce what is known as a recombinant form of the corresponding human protein in the animal's milk. We then purify the protein from the milk to obtain the therapeutic product, which is typically

administered to patients by injection. Our transgenic technology is protected by our leading patent position, which includes a U.S. patent, issued in 2006 and expiring in 2021, that covers the production of all therapeutic proteins in the milk of transgenic mammals.

Our transgenic production technology capabilities include the molecular biology expertise and intellectual property to generate transgenic animals, primarily goats, and, in some cases, rabbits, pigs, and cattle, that express a specific recombinant protein in their milk and to collect and purify the proteins once produced. We also have the necessary regulatory and clinical development experience required to navigate clinical trials and engage in commercial activities.

Our technology is well suited to large volume applications, particularly 100 kilograms or more per year, in comparison to traditional recombinant protein production systems. These advantages include significantly reduced capital expenditures, greater flexibility in expanding production capacity and lower unit production costs. In the case of certain complex proteins that do not express well in traditional systems, transgenic production may represent the only technologically and economically feasible method of commercial production. Many human plasma proteins are examples of recombinant proteins that may not express at economically viable levels in traditional systems.

We conduct our husbandry, breeding, milking and initial purification operations at our production facilities in central Massachusetts, where we have approximately 1,500 goats in a closed herd. Our goat husbandry operations include providing on site veterinary care. We have a biosecurity program that controls access to our site and includes barriers to provide separation of our animals from wildlife and the public. We also specify and carefully monitor feed quality. Milking is typically performed using modern milking and processing equipment. Filtration and purification are performed at our facilities, the facilities of our partners, or in contracted facilities. We have also established capacity in our Framingham, Massachusetts facilities for the purification of recombinant proteins suitable for clinical studies. We specifically do not permit the utilization of any of our transgenic or non-transgenic animals in the food chain, including their milk products.

While we have both the technical capability and the patent protection to work with a wide range of mammals, we typically utilize goats, as well as rabbits, pigs or cattle in our development programs. The species selected for a particular program will depend on a variety of factors, including the expected market size, desired herd size, and anticipated production level of the desired protein by the animal's mammary gland. We take great pride in the health and welfare of our animals. Our animal operations are subject to the review of our Institutional Animal Care and Use Committee and are accredited by the Association for the Assessment and Accreditation of Laboratory Animal Care International, or AAALAC, and we are registered with the U.S. Department of Agriculture, or USDA and the Office of Laboratory Animal Welfare of the National Institutes of Health, or OLAW.

We use microinjection or nuclear transfer technology to develop our transgenic animals. Microinjection involves injecting the desired DNA into a fertilized single cell embryo using a needle. In a number of our programs, including our lead program, ATryn®, we used microinjection to generate the initial transgenic animal, which we refer to as the founder animal. Nuclear transfer technology involves generating cells that have the specific DNA for expression of the target protein in milk and inserting the cell's DNA into an animal's ovum in place of the ovum's DNA. Once the ovum is activated, the embryo is implanted in the womb of a surrogate female animal. Nuclear transfer technology can offer more rapid development of large scale production capacity by producing a larger number of transgenic animals in one generation than through microinjection.

Advantages of Transgenic Production Technology

We believe our transgenic production technology provides significant advantages over traditional recombinant methods of therapeutic protein production, such as mammalian cell culture and bacterial systems, including:

- *Commercial Scale Production.* Transgenic production offers the ability to commercially produce therapeutic proteins for large volume indications while achieving consistent expression rates with complex molecules.

- *Lower Capital Investment.* Developing transgenic animals and maintaining appropriate production facilities can be accomplished with substantially lower capital investment than building a cell culture bioreactor production facility. In addition this is particularly important since commercial production capacity must be established before Phase III clinical studies are commenced.
- *Lower Cost of Goods.* Lower amortization from reduced capital investment, lower cost of consumable materials used in production and high productivity levels in protein production we believe will provide an assured lower cost of goods.
- *Flexible Production Capacity.* Transgenic production of recombinant proteins offers the ability to match production capacity to market demand once the first applicable transgenic animal is developed. If a product's market is larger than originally planned, the incremental investment to breed additional animals and collect and purify the related proteins is relatively small. In contrast, increasing production capacity of traditional cell culture and bacteria production networks requires the construction or acquisition of additional bioreactor space with unit costs similar to the original capital investment and with typical construction times of three to five years.
- *Glycosylation and ADCC Benefits.* Glycosylation refers to the process or result of adding sugars, or carbohydrates, to the amino acid structure of a protein during protein secretion. Glycosylation of therapeutic proteins produced in the mammary gland may have beneficial characteristics compared to those expressed in traditional cell culture and bacteria based technologies. Our production technology in many instances produces proteins with low fucose sugars which scientists believe can create enhanced ADCC. ADCC is the measure by which antibodies bind to target cells, making them more vulnerable to attack by immune cells. ADCC appears to be an important characteristic in the efficacy of many MAbs where targeted cell death is a desired outcome.

Collaborations

OVATION Pharmaceuticals

In June 2008, we entered into a collaboration agreement with OVATION Pharmaceuticals to develop and market ATryn® in the United States. The collaboration agreement includes the commercialization of ATryn® in the HD indication and the further development of ATryn® in AD indications. Under the terms of our agreement, OVATION is obligated to make milestone payments to us for a total of $9 million through approval of ATryn® for HD in the U.S., $ 5 million of which was received in 2008 and $4 million is expected to be received in the first quarter of 2009. The collaboration anticipates further development of ATryn® in larger market acquired deficiencies of antithrombin, such as the treatment of heparin resistance in patients undergoing surgery requiring cardiopulmonary bypass and the treatment of DIC associated with severe sepsis.

We are responsible for production of ATryn® and will receive a transfer price, including a margin, for commercial product, a royalty on net sales, $257 million in potential clinical, regulatory and sales milestone payments, including those already received, and payment for product used in clinical trials. Our agreement provides for OVATION to further develop ATryn® in AD and fund our anticipated costs of clinical development. OVATION will be responsible for sales and marketing of ATryn® in the U.S., including all launch activities, which are scheduled to commence in the second quarter of 2009.

LFB Biotechnologies

In September 2006, we entered into a collaboration agreement with LFB Biotechnologies to develop selected recombinant plasma proteins and MAbs using our transgenic production platform. LFB is a subsidiary of LFB S.A., a vertically integrated plasma fractionation company based in Paris, France that currently markets 19 plasma-derived products in the areas of hemostasis, anesthesia-intensive care and immunology. LFB S.A. is a for-profit company currently 100% owned by the French government. The first program in our collaboration

with LFB is for the development of rhFVIIa. We have subsequently added to the LFB collaboration programs to develop a recombinant form of human factor IX, an antibody to the CD20 immune system receptor, and recombinant human alpha-1 antitrypsin.

Our agreement with LFB provides that we are to share equally with LFB in the cost of the development and commercialization of each product and that we will be entitled to 50% of any profits derived from products developed through the collaboration provided we each contribute equally to the costs of their development. In the event that contributions to development are not equal, the profit allocation will be adjusted based on development costs incurred. Through 2008, LFB has contributed 85% of the costs of the joint venture and owns that same percentage of future profits, subject to our right to reestablish our 50% ownership by repaying LFB our share of the costs plus a specified premium that increases over time as clinical development progresses. Under the agreement, a joint steering committee of each company's representatives determines product development and commercialization plans. We are responsible for development of the production system for the products and retain exclusive commercial rights to the products in North America. LFB is responsible for clinical development and regulatory review of the programs in this collaboration, and has exclusive commercial rights in Europe. We hold co-exclusive rights with LFB in the rest of the world to all products developed through the collaboration. The initial term of the agreement is fifteen years, subject to extension or termination by mutual consent, and the terms for any product developed through the collaboration will continue until the later of the initial term or ten years beyond regulatory approval of that product. We have amended our agreement with LFB to establish LFB/GTC LLC as a separate legal entity for the joint venture. This amendment added LFB/GTC LLC as a party to the agreement and provided that rights to the intellectual property of the new joint venture will flow through this entity. All other terms and conditions remain the same.

In September 2006, LFB also purchased $25 million of our securities (see Note 3 to the Notes to Consolidated Financial Statements included in Item 8 of this Annual Report).

In December 2008, we completed a $15 million convertible debt financing with LFB (see Note 3 to the Notes to Consolidated Financial Statements included in Item 8 of this Annual Report).

LEO Pharma

In October 2005, we entered into a collaboration agreement with LEO for the commercialization of ATryn® in HD in Europe, Canada, and the Middle East and for its further development in AD indications. LEO selected DIC associated with severe sepsis as the first AD indication in which to conduct additional clinical studies under this collaboration.

LEO initiated a Phase II dose-ranging study in the DIC indication in 2007. In the third quarter of 2008, LEO advised us that, as a result of an internal re-assessment of their strategic priorities, they wished to enter in to negotiations to transfer the ATryn® program to us or an alternate partner. Pending any such transfer, further patients are not being enrolled in the study at this time. LEO has made it clear that their decision was not based on any safety or efficacy issues. We are currently engaged in a dispute resolution process with LEO, as described under Item 3 in this Annual Report.

Patents and Proprietary Rights

We currently hold 24 issued or allowed U.S. patents and 202 corresponding foreign patents. We have received a U.S. patent with claim coverage for the production of therapeutic proteins in the mammary glands of transgenic mammals. This patent has an expiration date of 2021. Our other patents generally expire between 2010 and 2023. In accordance with ongoing research and development efforts, we have 29 pending U.S. patent applications and 81 corresponding foreign applications covering relevant and newly developed portions of our transgenic technology. Several of these pending applications are included in various cross-licensing or out-licensing arrangements with other companies that in turn provide us access to their proprietary technologies. We have granted limited access to our technology to Pharming Group, N.V., PharmAthene and JCOM. Recently issued U.S. patents provide us with claim coverage for protein purification from the milk of transgenic animals, the production of monoclonal and assembled antibodies at commercial levels in the milk of transgenic mammals,

the production of recombinant antithrombin in the milk of transgenic goats and the production of prolactin in the milk of transgenic animals. Pursuant to the December 2008 convertible debt financing, LFB has a first lien on all of our intellectual property, including trademarks, not otherwise assigned to third parties, and GE Capital has a second lien on all of our intellectual property, including trademarks, not otherwise assigned to third parties. These liens do not prevent us from licensing technology in the ordinary course of business.

In addition, we hold exclusive and non-exclusive licenses from Genzyme Corporation, Biogen-Idec, Inc., and other individuals and corporations to rights under a number of issued patents and patent applications in the U.S. and the corresponding cases abroad for a variety of technologies enabling the transgenic production of proteins in the milk of non-human animals.

We have exclusive and nonexclusive licenses to specific technologies owned by other parties. Some of the licenses require us to pay royalties on sales of products which may be derived from or produced using the licensed technology. These licenses generally extend for the life of any applicable patent. We have concluded an extensive cross-licensing arrangement with Pharming providing broad access to its transgenic cattle platform as well as some additional nuclear transfer technology. We have also obtained a non-exclusive license to nuclear transfer technology from Start Licensing Inc.

We obtained a license from ProGenetics, LLC, granting us exclusive rights for North America, Europe and Japan to commercially develop recombinant human factor VIII and recombinant human factor IX. LFB subsequently purchased a 50% share of these rights, and these rights have been assigned to the LFB joint venture. We granted ProGenetics a non-exclusive license to our patent for the transgenic expression of therapeutic proteins in milk in the United States to enable the commercial development of these products outside of our territories of North America, Europe and Japan.

We rely upon certain proprietary trade secrets, know-how and continuing technological advances to develop and maintain our competitive position. In an effort to maintain the confidentiality and ownership of trade secrets and proprietary information, we generally require employees, consultants and collaborators to execute confidentiality and invention assignment agreements upon commencement of a relationship with us.

Competition

Competition in the biotechnology and pharmaceutical industries is intense and comes from many and varied sources. We experience significant competition from specialized biotechnology firms and large pharmaceutical companies in the U.S., Europe and elsewhere. Some of our competitors have substantially greater financial, marketing, research and development and human resources than we have. Most large pharmaceutical and biotechnology companies have considerable experience in undertaking clinical trials and in obtaining regulatory approval to market pharmaceutical products. In addition to company and industry level competition, our proprietary programs face particular competitive challenges.

Competition for our lead product candidate ATryn® comes from a number of companies internationally producing and marketing human antithrombin sourced from the fractionation of human plasma. CSL Behring's antithrombin has a significant share of this market worldwide, but is not approved in the U.S. Talecris, which has a pending agreement to merge with CSL, is the only company that has commercially available fractionated antithrombin that is approved for sale in the U.S. Talecris' U.S. sales are a small portion of the worldwide antithrombin market. There are many providers of plasma-derived antithrombin in Europe, including Octopharma, Grifols, Baxter International, Pfizer, Inc., CSL Behring and LFB. A Grifols plasma-derived antithrombin product is in clinical studies to support a planned request for approval with the FDA. As part of the orphan drug designation of ATryn®, we have been granted market exclusivity for seven years for the treatment of patients in the HD indication.

In 2007 Talecris disclosed that its sales of their plasma-derived AAT product, Prolastin®, were $277 million in 2008. We estimate that plasma-sourced AAT products currently generate worldwide annual sales of approximately $400 million.

Novo Nordisk is the manufacturer of the only available recombinant form of factor VIIa, NovoSeven®, which is approved for the treatment of hemophilia patients with inhibitors to factors VIII and IX. There are insignificant sales of various plasma-derived factor VIIa products for the treatment of these hemophilia patients. The NovoSeven® patents expire in 2011.

An existing rhFIX product marketed as BeneFIX® by Wyeth is commercially available with estimated 2008 annual sales of $587 million. One estimate projects that the total annual market size for BeneFIX® could be $1 billion within the next four years.

There are many companies, including biotechnology and pharmaceutical companies, which are actively engaged in seeking efficient methods of producing proteins for therapeutic applications. These include companies that are developing transgenic technology using various mammalian, plant and avian systems, as well as many companies that are building their own cell-culture-based production systems or other recombinant protein production methods, and contract manufacturers who are using those systems to produce proteins for others. Any of these companies could become competitors.

Government Regulation

The manufacturing and marketing of our potential products and certain areas of research related to them are subject to regulation by federal and state governmental authorities in the U.S., including the FDA, the USDA and the Environmental Protection Agency. Comparable authorities are involved in other countries, including the EMEA in Europe. As of February 2009, ATryn® is the only transgenically produced drug approved for marketing in Europe and the U.S.

Legal requirements for the investigation and commercialization of drug products and medical devices are set forth in the Federal Food, Drug and Cosmetic Act and regulations issued thereunder. While similar in many respects, legal requirements for the development and licensure of biological products, including transgenic products, are set forth in the Public Health Service Act, or PHSA, and regulations issued under that statute. As with drug products, these regulations require FDA approval prior to marketing. This approval is based on the manufacturer's demonstration that the product is safe and effective for its labeled or indicated uses. The demonstration of safety and efficacy, is subject to a thorough review by FDA and consists of both preclinical laboratory and animal studies, which must demonstrate that the drug or biological product is sufficiently safe to be tested in humans, and extensive human clinical trials, which establish the product's safety and efficacy in humans at the doses it will be administered and for the uses for which it will be labeled and marketed. This testing is both lengthy and expensive, and its outcome is frequently uncertain. In general, following testing in animals to establish that the drug is sufficiently safe for human testing, manufacturers apply for permission to study the drug in humans through the filing of an IND application which contains both the results of the animal testing as well as the plan or protocol for testing the drug in humans. Testing in humans usually encompasses three phases (I, II and III). Phase I studies, frequently conducted in healthy subjects, establish preliminary safety and kinetics in humans; Phase II studies are usually controlled and provide preliminary findings of efficacy and safety, while Phase III studies consist of much larger controlled trials and are used to establish the necessary proof of efficacy to support marketing. All testing in humans is subject to FDA oversight, and may be suspended or delayed if the agency determines that subjects may experience any unanticipated or unreasonable risks.

Following a manufacturer's conclusion of the testing paradigm, the details of which may differ depending on the type of drug, the medical need for it, and the seriousness of the condition it is intended to treat, the data is compiled by the manufacturer into either a New Drug Application, or NDA, for new drugs, or a Biologics License Application, or BLA for biological products, in accordance with the classification for the molecule determined by the FDA, and submitted for review. In addition, manufacturers are required to include extensive data regarding the composition and manufacture of the product to assure its purity, potency and quality. The FDA may request additional information or data from the manufacturer, and following its review will either approve or disapprove the application. As part of a decision to approve the drug, the FDA will approve product labeling, setting forth the use or uses which have been shown to be safe and efficacious, summaries of the clinical studies, dosing information, and extensive information presented hierarchically about potential risks. It may also require

further testing as a condition of approval (referred to as Phase IV) as well as inform the manufacturer of certain limitations it believes are appropriate for product promotion. The approval process is comparable in Western Europe and other modern countries, such as Japan, with respect to the need for both safety and efficacy to be demonstrated through rigorous clinical trials.

For technologies such as ours where animals incorporate additional DNA into their genome, the FDA has established guidance that New Animal Drug Applications shall be submitted to permit review by the Center for Veterinary Medicine. This NADA review is focused on the control of the transgene, the health of the animals involved, and any environmental impact. The ATryn® program was reviewed under an NADA, and all elements of our care and use of animals program were deemed to meet the standards required for approval.

Following marketing approval, the FDA continues to regulate drug and biological products extensively. Manufacturers are required to supply the agency with reports of all adverse events submitted to them, to report product defects, to submit to routine facility inspections, and to notify the agency of any planned product changes, many of which may also require prior approval. The failure to meet continuing regulatory requirements can result in administrative and legal sanctions, such as product recalls, requests to issue new information to medical practitioners, and in severe cases, product withdrawals, seizures, injunctions, and criminal prosecutions. All marketing is also subject to continuing FDA monitoring which, if found deficient or in violation of requirements, may result in demands for corrective measures as well as potential imposition of the same sanctions. More recently, pharmaceutical marketing violations by several companies have been subject to extensive and serious sanctions of the Food and Drug Control Administration, or FDCA, the Medicare/Medicaid anti-kickback legislation and the False Claims Act by the federal and various state attorneys general and the Health and Human Services Office of Inspector General, including the imposition of both civil and criminal fines, the application of corporate integrity agreements, and in the most serious cases, potential disqualification from providing product to the agencies of the federal government.

Research and Development Costs

During 2008, 2007 and 2006, we incurred development expenses of $21 million, net of $5.1 million of funding from LFB, $28.9 million, net of $1.2 million of funding from LFB and $25.4 million, respectively, including preclinical and clinical development expenses related to our proprietary programs. Of the total spent on research and development, $15.5 million, $21 million and $20.3 million, was for costs spent on the ATryn® development program in fiscal years 2008, 2007 and 2006, respectively, which included manufacturing costs for our U.S. clinical trial, manufacturing costs of clinical material in excess or the maximum selling price to LEO as well as process development and validation costs for scale up of the ATryn® manufacturing process. These costs include labor, materials, supplies and overhead, as well as certain subcontracted service costs. Also included are the costs of operating the transgenic production facility such as feed and bedding, veterinary costs and utilities.

New Zealand Goats

Since 1993, we have maintained a reserve herd of goats in New Zealand as security and as a backup herd for our goats in the U.S. We have resourced our goats from New Zealand because of the exceptional record of low levels of adventitious organisms in New Zealand livestock.

Employees

As of December 28, 2008, we employed 159 people, including 6 part-time and temporary employees. Of our total employees, 86 were engaged in farm operations, clarification processes, quality assurance and control, 15 were engaged in research and development and 58 were engaged in administration, business development and marketing. Of our employees, approximately 15 have Ph.D. degrees and 3 have D.V.M. degrees. None of our employees are covered by collective bargaining agreements. We believe our employee relations are satisfactory.

Executive Officers

Our executive officers and their respective ages and positions as of February 23, 2009 are as follows:

Name	Age	Position
Geoffrey F. Cox, Ph.D.	65	Chairman of the Board, President and Chief Executive Officer
John B. Green	54	Senior Vice President, Chief Financial Officer and Treasurer
Harry M. Meade, Ph.D.	62	Senior Vice President, Research and Development
Richard A. Scotland.	53	Senior Vice President, Regulatory Affairs
Daniel S. Woloshen	60	Senior Vice President and General Counsel

Dr. Cox was appointed Chairman of the Board, President and Chief Executive Officer in July 2001. From 1997 to 2001, Dr. Cox was Chairman and Chief Executive Officer of Aronex Pharmaceuticals, Inc., a biotechnology company. From 1984 to 1997, Dr. Cox was employed by Genzyme Corporation, where he most recently served as Executive Vice President, responsible for operations and the pharmaceutical, diagnostic and genetics business units. Prior to joining Genzyme, Dr. Cox was General Manager of the UK manufacturing operations for Gist-Brocades. Dr. Cox also serves as non-executive Chairman of the Board for Nabi Biopharmaceuticals, and serves on the Board of the Biotechnology Industry Organization and the Board of the Massachusetts Biotechnology Council. Dr. Cox received a Ph.D. in Biochemistry from the University of East Anglia U.K. and a BSc (Hons) in Biochemistry from the University of Birmingham U.K.

Mr. Green was appointed Senior Vice President in May 2002, having previously served as Vice President since 1994. Mr. Green has also served as our Chief Financial Officer since December 1994 and Treasurer since August 1997. Prior to joining us, Mr. Green was Vice President and Assistant Treasurer of TSI Corporation from December 1989 until our acquisition of TSI in 1994. Mr. Green is a Certified Public Accountant (CPA) with over 30 years of financial experience, including 20 within the biotechnology industry as Chief Financial Officer of GTC and Vice President and Assistant Treasurer for TSI Corporation. Mr. Green received a Master's degree in Business Administration from Boston University Graduate School of Management and a Bachelor's degree from the College of the Holy Cross.

Dr. Meade was appointed Senior Vice President of Research and Development in May 2002. From 1994 to 2002, Dr. Meade was our Vice President of Transgenics Research, having served as Research Director since May 1993. Prior to joining us, Dr. Meade was a Scientific Fellow at Genzyme, where he was responsible for directing the transgenic molecular biology program. From 1981 to March 1990, Dr. Meade was a Senior Scientist at Biogen, Inc., where he helped develop the technology used for protein production in milk and was a named inventor on the first issued patent covering the related protein production process. Dr. Meade received his Ph.D. in Biology from the Massachusetts Institute of Technology and completed his post-doctoral studies at Harvard University. He holds Bachelor's degrees in Chemistry and Electrical Engineering from Union College.

Mr. Scotland joined GTC Biotherapeutics in 2002 and holds the position of Senior Vice President, Regulatory Affairs. Mr. Scotland is responsible for directing worldwide regulatory activities pertaining to the development of therapeutic proteins derived from the milk of transgenic animals. Mr. Scotland has over 25 years of regulatory affairs experience with various biotechnology and pharmaceutical companies, including Serono Laboratories, Genzyme Corporation and Astra Pharmaceuticals. Mr. Scotland holds a Bachelor's degree in Biology from St. Joseph's College in North Windham, Maine.

Mr. Woloshen was appointed Senior Vice President and General Counsel in May 2002, having previously served as Vice President and General Counsel since August 1999. Prior to joining us, Mr. Woloshen served as Vice President and General Counsel of Philips Medical Systems North America from April 1989 to July 1999. Mr. Woloshen received a Juris Doctor degree from Boston College Law School and holds a Bachelor's degree from Colby College.

Available Information

Our internet website is www.gtc-bio.com and through the "Investor Information" portion of the website, investors may access, free of charge, our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, proxy statements on Schedule 14A and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the Securities and Exchange Commission. Information on our Investor Information page and on our website is not part of this Annual Report or any of our other securities filings unless specifically incorporated herein by reference.

ITEM 1A. RISK FACTORS

The following are certain factors that could affect our future results. They should be considered in connection with evaluating forward-looking statements made by us because these factors could cause actual outcomes and results to differ materially from the outcomes and results as expressed in those forward-looking statements.

RISKS RELATED TO OUR BUSINESS

We expect to continue to incur significant operating losses for the next several years and we may never become profitable.

We have had operating losses since our inception, and we expect losses to continue for the next several years. From our inception in 1993 to December 28, 2008, we have incurred cumulative losses of approximately $304 million. These losses have resulted principally from the costs of our research and development activities. Our net losses for fiscal years 2008, 2007 and 2006 have been $22.7 million, $36.3 million and $35.3 million, respectively. We expect to continue incurring significant operating losses for at least the next several years. We may never receive material revenues from product sales or become profitable.

Our current resources are only sufficient to fund our operations in the short term, which raises substantial doubt about our ability to continue as a going concern.

As of December 28, 2008, we had $11.6 million in cash and cash equivalents, which were offset by our $16.1 million in current liabilities. We expect our current cash resources and potential future cash payments from existing collaborations and licensing programs to be sufficient to fund operations into the second quarter of 2009. We have received an audit report from our independent registered public accounting firm containing an explanatory paragraph stating that our historical recurring losses from operations and limited funds raise substantial doubt about our ability to continue as a going concern. We will have to obtain additional equity or debt financing or payments from new and existing partnering collaborations, or funding from a combination of these sources, to fund a sufficient number of our clinical development plans through to regulatory approval to allow us to be self-sustaining.

We may be unable to raise the additional capital needed to develop and commercialize our product programs successfully.

We will need additional capital to fund our operations, including research and development, manufacturing and commercialization. In order to develop and bring our transgenically produced products to market, we and our collaboration partners must commit substantial resources to costly and time-consuming research, preclinical testing and clinical trials. If we do not have or cannot raise additional capital when needed, we would be forced to delay, scale back or eliminate one or more of our research and development programs of our farm operations.

Our drug development programs and the further development of ATryn® will require substantial additional cash to fund expenses that we will incur in connection with preclinical studies and clinical trials, regulatory review, manufacturing and sales and marketing efforts. Our cash requirements may vary materially from those now planned, depending upon the results of our research and development programs, competitive and technological

advances, the terms of future collaborations, regulatory requirements and other factors. We expect we will need to obtain additional financing, through public or private sources, including debt or equity financing, in addition to any funding obtained through collaborative or other arrangements with corporate partners. Depending on the state of the capital markets, interest rates, our financial profile and other factors at that time, we may not be able to obtain adequate funds on acceptable terms when needed. If we raise capital through the sale of equity, or securities convertible into equity, existing shareholders' proportionate ownership in us will be reduced.

Our collaboration partners may fail to perform satisfactorily or may terminate our collaboration agreements.

We are dependent on our collaboration partners for the development and commercialization of our approved product and our lead product candidates. We do not have adequate resources to develop our products and product candidates on our own. We also have neither the experience nor capabilities to sell, market or distribute products. We currently have a collaboration agreement with OVATION, which has recently agreed to be acquired by Lundbeck, to develop and market ATryn® and a collaboration agreement with LFB to develop selected recombinant plasma proteins and MAbs. We are in the process of trying to transition our collaboration with LEO to another party. We also plan to enter into additional collaborations with other partners to develop and commercialize current and future products and product candidates. The performance of our collaboration partners is not within our control. For example,

- we may not be able to ensure that our collaboration partners dedicate sufficient time and resources to successfully meet their obligations under our collaboration agreements;
- disputes may arise between us and our partners that may result in the delay or termination of the development or commercialization of products or product candidates or that may subject us to costly litigation or arbitration;
- our collaboration partners may experience financial difficulties or undergo business combinations or significant changes in corporate strategy that may adversely affect their ability or willingness to meet their obligations under our collaboration agreements; and
- our collaboration partners may not adequately maintain and protect, or may improperly use, our proprietary information, which could jeopardize our intellectual property rights or subject us to costly litigation or arbitration.

We depend on collaboration agreements for our current revenue and significant funding.

Our revenues and business strategy depend largely on our entering into additional development and marketing agreements with third parties as well as existing agreements for our own therapeutic compounds. We may not be able to establish these agreements on commercially acceptable terms, if at all, depending on the market position of our technology and our compounds. The willingness of potential collaborators to enter into agreements with us depends on factors such as the perceived technological or economic advantages of transgenic production and our ability to structure a mutually acceptable collaboration arrangement. For existing and future development agreements, the collaborations may ultimately be unsuccessful, our partners could terminate the agreements or the agreements could expire before meaningful developmental milestones are reached. Depending upon the terms of any future collaborations, our role in the collaboration will often be limited to the production aspects of the proteins. As a result, we may also be dependent on collaborators for other aspects of the development of any transgenically produced product, including preclinical and clinical testing and regulatory approval, and marketing and distribution.

The majority of our collaborations to date have been external programs that involve proteins proprietary to our partners. Much of the continuing revenue, if any, that we may receive under these collaborations will depend upon our partners' willingness and ability to successfully develop and commercially introduce, market and sell the version of the collaborator's product derived from our transgenic production systems. Our partners may

choose competitive production technologies or competitive products outside of their collaborations with us, which could have a material adverse effect on our business. The failure of any external collaboration could have a material adverse effect on our business.

We may fail to obtain the necessary regulatory approval to market and sell our transgenically produced products in the United States or in other countries.

Before we can market or sell any transgenically produced drug or biological products that we or our collaborators develop, we must receive regulatory approvals from federal, state and local governmental authorities, including the FDA and corresponding agencies in other countries, such as the European Medicines Agency, or EMEA, in Europe. We received our only regulatory approvals of any of our transgenically produced products in August 2006 from the European Commission for use of ATryn® as a prophylactic treatment of patients with hereditary antithrombin deficiency undergoing surgical procedures and from the FDA in February 2009 for surgical procedures and childbirth. Our Marketing Authorization Application for ATryn® was approved by the European Commission under exceptional circumstances, meaning that the license must be renewed on an annual basis as opposed to every five years, with certain post approval obligations that must be fulfilled to maintain approval. In addition, continuing marketing authorization approval must be obtained on an annual basis. The required regulatory approvals process for our transgenically produced products may take several years to complete and is expensive and uncertain. It is possible that the FDA or any other regulatory authority may not act quickly or favorably on our requests for approval or may require us to provide additional data that we may not have then available. For example, the FDA may impose restrictions and demands on our clinical trials that require additional resources and result in unexpected delays. In addition, the FDA may require us to conduct further clinical trials and post-marketing testing and surveillance to monitor the effects of approved products. The FDA or other regulatory authorities may also place conditions on approval that could restrict the commercial applications of such products.

Failure to comply with extensive FDA or similar regulations may result in delay, suspension or cancellation of a trial or a regulatory authority's refusal to accept test results. Regulatory authorities may have varying interpretations of our pre-clinical and clinical trial data, which could delay, limit or prevent regulatory approval or clearance. Because transgenically produced products represent novel therapeutic products, the process for regulatory approval is unproven. There may be additional delays in regulatory approval due to issues arising from the breeding of transgenic animals and the use of proteins derived from them. Any delays or difficulties in obtaining regulatory approval or clearance for transgenically produced products may:

- adversely affect the marketing of any transgenically produced products we or our collaborators develop;
- impose significant additional costs on us or our collaborators;
- diminish any competitive advantages that we or our collaborators may attain; and
- limit our ability to receive royalties and generate revenue and profits.

If we do not receive regulatory approvals for our transgenically produced products in a timely manner, we will not be able to commercialize our products, or their commercialization may be limited or delayed and, therefore, our business and stock price will suffer.

In addition to traditional regulatory review by the FDA, the FDA established guidance for New Animal Drug Applications to be submitted to permit review by the Center for Veterinary Medicine of technologies such as ours where animals have additional DNA incorporated into their genome. This NADA review is focused on control of the transgene, the health of the animals involved, and any environmental impact. Although the ATryn® program was reviewed and approved under an NADA and all elements of our care and use of animals were deemed to meet the standards required for approval, there is no guarantee that we will continue to meet NADA standards in future periods or for future products.

Even if we receive regulatory approval for our transgenically produced products, the FDA or similar agencies in other countries may impose limitations on the indicated uses for which our products may be marketed and sold. These limitations could reduce the size of the potential market for a product. Failure to comply with applicable FDA and other regulatory requirements could result in, among other things, warning letters, fines, injunctions, civil penalties, recall or seizure of products, total or partial suspension of production, refusal of the government to renew our marketing applications and criminal prosecution.

Our clinical trials of our transgenically produced products may be unsuccessful or delayed, which may prevent us from meeting our anticipated development timeline.

We and our collaborators must demonstrate through preclinical and clinical trials that our transgenically produced products are safe and effective for use in humans. Clinical trials are expensive and may take several years. Several factors could prevent or delay completion of these trials, including an inability to enroll the required number of patients or demonstrate adequately the safety or efficacy of the product for humans. If safety concerns develop, regulatory authorities could stop or delay our trials. Furthermore, the results from early clinical trials are often not predictive of results in later clinical trials.

To our knowledge, Pharming is the only other entity to have completed human clinical trials of a transgenically produced product. If we are unable to complete all clinical trials and to satisfy other requirements that may be required by the FDA, or the EMEA for expanded indications of ATryn®, or if any of our other transgenically produced proteins in development are not proved to be safe or effective to the satisfaction of regulatory authorities, it would have a material adverse effect on our business and operations.

Any transgenically produced products for which we obtain regulatory approval will be subject to continuing review and extensive regulatory requirements, which could affect their manufacture and marketing.

If and when the FDA or other foreign agencies approve any of our transgenically produced products under development, the manufacture and marketing of these products will be subject to continuing regulation and product approvals may be withdrawn if problems occur after initial approval. Post-approval regulation includes compliance with current Quality Systems Regulations and Good Manufacturing Practices, known as QSR/GMP, adverse event reporting requirements and prohibitions on promoting a product for unapproved uses. We will also be required to obtain additional approvals for any significant alterations in the product's labeling or manufacturing process. Enforcement actions resulting from failure to comply with QSR/GMP requirements could result in fines, suspensions of approvals, recalls of products, operating restrictions and criminal prosecutions, and affect the manufacture and marketing of our transgenically produced products. The FDA or other regulatory agencies could withdraw a previously approved product from the market upon receipt of newly discovered information, including a failure to comply with regulatory requirements and the occurrence of unanticipated problems with products following approval. Any of these withdrawals could adversely affect our operating results.

We have limited manufacturing capability and may be required to rely on third party contract manufacturers to purify and formulate our transgenically produced products.

We currently have the capability to purify pre-clinical and clinical trial quantities of our transgenically produced products up to and including Phase II trials. We also rely upon third party manufacturers to purify and formulate significant pre-clinical, clinical and commercial quantities of our transgenically produced products. We depend on these third party manufacturers to perform their obligations in a timely manner and in accordance with applicable government regulations in order to conduct our clinical trials or commercialize any of our products. For example, we had to write off $2.9 million of ATryn® inventory in 2007 which was rendered unusable as a result of the fill/finish process conducted at a U.S.-based fill/finish contractor. We have terminated our contract with that contractor and now are only using MedImmune (Holland) for these services. There are very few third party manufacturers that have sufficient production capacity to manufacture all of our products either for our clinical trials or on a commercial scale. Our third party manufacturers may encounter difficulties, including problems involving:

- inconsistent production yields;

- poor quality control and assurance or inadequate process controls;
- lack of compliance with FDA, EMEA and other regulations; and
- high production costs.

These contract manufacturers may not be able to manufacture our products at a cost or in quantities necessary to make them commercially viable. If we are unable to enter into agreements with additional manufacturers on commercially reasonable terms, or if there is poor performance on the part of our third party manufacturers, we may not be able to complete development of, or market, our transgenically produced products.

We have contracted with Lonza Biologics for large scale purification and with Medimmune (Holland) for fill/ finish services of our lead product, ATryn®. Although we have identified possible alternative suppliers with respect to these services for this product, interruptions in these services and the process of changing to an alternative manufacturer could have a material adverse effect on our timely ability to manufacture bulk delivery of ATryn® for delivery to our collaborators or to market distribution after regulatory approval.

Transgenically produced products may never become commercially successful.

Even if our transgenically produced products are successfully developed and approved by the FDA and foreign regulatory agencies, they may not enjoy commercial acceptance or success, which would adversely affect our business and results of operations. Several factors could limit our success, including:

- limited market acceptance among patients, physicians, medical centers and third party payors, including acceptance of products transgenically produced from animals;
- our inability to access a sales force capable of marketing the product, either through a third party contract sales force or by establishing our own internal sales force;
- our inability to supply a sufficient amount of product to meet market demand;
- the number and relative efficacy of competitive products that may subsequently enter the market; and
- the relative risk-benefit profile and cost-effectiveness of transgenically produced product designed to replace or supplement currently marketed non-transgenically produced products.

In addition, it is possible that we or our collaborative partners will be unsuccessful in developing, marketing or implementing a commercialization strategy for any transgenically produced products.

Our business may fail due to intense competition in our industry.

The industry in which we operate is highly competitive and may become even more so. Some of our competitors have greater financial and human resources and more experience in research and development than we have. We will need to continue to devote substantial efforts and expense in research and development to maintain a competitive position for our transgenic production technology and potential product offerings. It is also possible that others will develop alternative technologies or products that will render our proposed products or technologies obsolete. We may encounter significant competition for our protein development and production capabilities from other companies. In addition, our potential transgenic production capabilities may face significant competition from biological products manufactured in cell culture or by other traditional protein production methods. Our business will also compete against other companies whose business is dedicated to offering transgenic production and with prospective customers or collaborators who decide to pursue such transgenic production internally. Competitors that complete clinical trials, obtain regulatory approvals and begin commercial sales of their products before us will enjoy a significant competitive advantage. We anticipate that we will face increased competition in the future as new companies enter the market and alternative technologies become available.

For ATryn®, a number of companies internationally produce and market antithrombin derived from human plasma. CSL Behring's product has a significant share of the worldwide market, but is not approved for sale in the U.S. Talecris, which purchased Bayer's plasma business and is being acquired by CSL, has a commercially available fractionated antithrombin product that is approved for sale in the U.S. Other companies, including Octapharma, CSL Behring, Grifols, Kedrion, Baxter International and LFB supply the European market with plasma-derived antithrombin products, none of which have been approved throughout the European Union.

Like antithrombin, the alpha-1 antitrypsin sold today is derived from human plasma. Talecris has a significant presence in the U.S. with an alpha-1 antitrypsin product called Prolastin® which is approved for chronic use in patients with a genetic deficiency of alpha-1 antitrypsin who are prone to pulmonary disorders such as emphysema.

Novo Nordisk is the manufacturer of the only available recombinant form of factor VIIa, NovoSeven®, which is approved for the treatment of hemophilia patients with inhibitors to factors VIII and IX. There are insignificant sales of various plasma-derived factor VIIa products for the treatment of these hemophilia patients. The NovoSeven® patents expire in 2011.

To the extent that a market develops for transgenically produced therapeutic products generally, we may compete with other transgenic technology companies. Pharming and BioProtein Technologies are other companies known to us that are extensively engaged in the application of transgenic technology in mammals for the production of proteins for therapeutic use in humans. Pharming, based in the Netherlands, is primarily engaged in the development of recombinant proteins in the milk of transgenic cows and rabbits. Pharming reports that it has one product that has been submitted for review by the EMEA. Pharming has also submitted a request to the FDA to recognize their lactoferrin product as being safe for nutritional applications. BioProtein Technologies is a contract manufacturing organization specializing in the production of human therapeutic proteins and vaccines in the milk of transgenic rabbits. There are also other companies seeking to develop transgenic technology in animals and in plants, which may be competitive with our technology with respect to our patents and proprietary rights as discussed further below. In addition, it is possible that research and discoveries by others could render our transgenic technology obsolete or noncompetitive as a method of production for protein-based therapeutic products.

We may face public concerns about genetic engineering in animals.

Our activities involve genetic engineering in animals. The success of our potential commercial products will depend in part on public acceptance of the use of genetic engineering. Public attitudes may be influenced by claims and perceptions that these types of activities are unsafe and our products may not gain the acceptance of the public or the medical community. Negative public reaction to genetic engineering activities in general could result in greater restrictive legislation and regulations involving nuclear transfer and other methodologies which could impede our ability to conduct our business efficiently, delay preclinical studies or future clinical trials, or prevent us or our partners from obtaining regulatory approvals or commercializing transgenically produced products.

Our transgenically produced products may be subject to technology risks that may restrict or prevent their development and commercialization.

Developing products based on transgenic technology is subject to significant development risks. Each DNA construct is unique and it is possible that it might not be expressed in the transgenic animal's milk at a level that is commercially viable. Purifying the recombinant protein out of the milk to use as a biotherapeutic may be too difficult to be commercially feasible. In addition, production of the recombinant protein may have negative effects on the health of either the mammary gland or more systematically on the animal as a whole. This would compromise the ability of the animal to produce the recombinant protein. Directing the mammary gland to produce additional proteins in the milk could negatively affect lactation, thereby shutting down milk production. The mammary gland may also modify a protein in such a manner that it is non-functional or harmful in humans. It is also possible that there may be disease agents present in the animals that would prevent the use of products

derived from these animals. If an as yet unknown disease was identified that could not be effectively mitigated, government agencies may confiscate or destroy the animals, or prevent the utilization of their milk. Any of these governmental actions would prevent the use of the recombinant proteins.

We depend on patents and proprietary rights that may fail to protect our business.

Our success will partly depend on our ability to obtain and maintain patent or other proprietary protection for our technologies, products and processes such as:

- compositions of matter or processes;
- processes developed by our employees; or
- uses of compositions of matter discovered through our technology.

We may not be able to obtain the necessary proprietary protection. Our success will also depend on our ability to operate without infringing the proprietary rights of other parties. Legal standards relating to the validity of patents covering pharmaceutical and biotechnological inventions and the scope of claims made under these patents are still developing. There is no consistent policy regarding the breadth of claims allowed in biotechnology patents. The patent position of a biotechnology company is susceptible to uncertainty and involves complex legal and factual questions.

We hold 24 issued or allowed U.S. patents and 202 corresponding foreign patents. Our patents generally expire between 2013 and 2015, with the exception being a recently issued patent in the United States, which expires in 2021. This patent provides us with claim coverage for the production of therapeutic proteins in the mammary glands of transgenic mammals. One in-licensed European patent, pertaining to transgenic animals secreting proteins in milk, expired in 2006. In accordance with ongoing research and development efforts, we have 29 pending U.S. patent applications and 81 corresponding foreign applications covering relevant and newly developed portions of our transgenic technology. Several of these pending applications are included in various cross-licensing or out-licensing arrangements with other companies that in turn provide access to their proprietary technologies. Specifically we have cross-licensed our proprietary technology for the production of proteins in milk to Pharming. Other technologies for which we hold existing patents include: protein purification from the milk of transgenic animals, the production of monoclonal and assembled antibodies at commercial levels in the milk of transgenic mammals and the production of recombinant antithrombin in the milk of transgenic goats. We cannot be certain that we will receive issued patents based on pending or future applications. Our issued patents may not contain claims sufficiently broad to protect us against competitors with similar technology. Additionally, our patents, our partners' patents and patents for which we have license rights may be challenged, narrowed, invalidated or circumvented. Furthermore, rights granted under patents may not provide us with any competitive advantage.

We may have to initiate arbitration or litigation to enforce our patent and license rights. If our competitors file patent applications that claim technology also claimed by us, we may have to participate in interference or opposition proceedings to determine the priority of invention. An adverse outcome could subject us to significant liabilities to third parties and require us to cease using the technology or to license the disputed rights from third parties. We may not be able to obtain any required licenses on commercially acceptable terms or at all.

The cost to us of any litigation or proceeding relating to patent rights, even if resolved in our favor, could be substantial. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because of their substantially greater resources. Uncertainties resulting from the initiation and continuation of any pending patent or related litigation could have a material adverse effect on our ability to compete in the marketplace. An unfavorable result could subject us to significant liabilities to third parties, require us to cease using the affected processes or require us to license the disputed rights from third parties. For example, a key nuclear transfer patent that we licensed from a third party was invalidated in favor of a patent application now licensed to Start Licensing, Inc. In response to the ultimate resolution of that invalidation, we

obtained a non-exclusive license from Start Licensing, Inc. for patents and patent applications developed to apply nuclear transfer to the production of therapeutic proteins in the milk of transgenic animals. If, unlike the Start Licensing example, we could not obtain a license to patented technology we need, or could only obtain a license on terms we consider to be unacceptable, or if we were unable to design our products or processes to avoid infringement of such patented technology, our business would be harmed.

We rely on certain proprietary trade secrets and know-how that are not patentable. We have taken measures to protect our unpatented trade secrets and know-how, including having our employees, consultants and some contractors execute confidentiality agreements. These agreements could be breached. If so, it is possible that our remedies for a given breach might be inadequate. It is also possible that competitors emerge who could independently develop or discover our trade secrets or that the trade secrets could otherwise become known.

We may not be able to recover from any catastrophic event affecting our animals or facilities.

While we have measures in place to minimize and recover from catastrophic events that may substantially destroy our animal herd(s), these measures may not be adequate to recover our production processes quickly enough to support critical timelines, collaborator needs or market demands. These catastrophic events may include animal diseases that breach our biosecurity measures or weather events such as tornadoes, earthquakes or fires. In addition, these catastrophic events may render some or all of the products at the affected facilities unusable.

Successful commercialization of our products will depend on obtaining coverage and reimbursement for use of the products from third-party payors.

Sales of pharmaceutical products depend largely on the reimbursement of patients' medical expenses by government health care programs and private health insurers. It is possible that third-party payors will not reimburse sales of our transgenically produced products. Reimbursement by third-party payors depends on a number of factors, including the payor's determination that use of the product is safe and effective, not experimental or investigational, medically necessary, appropriate for the specific patient and cost-effective. Reimbursement in the United States or foreign countries may not be available or maintained for any of our products. If we do not obtain approvals for adequate third-party reimbursements, we may not be able to establish or maintain price levels sufficient to realize an appropriate return on our or our partners' investment in product development. Any limits on reimbursement available from third-party payors may reduce the demand for, or negatively affect the price of, our or our partners' products. Without the financial support of the government or third-party insurers, the market for transgenically produced products will be limited.

The U.S. federal government and private insurers are continually working on ways to contain health care costs, particularly by limiting both coverage and the level of reimbursement for new therapeutic products. The government or private insurers may institute future price controls and other cost-containment measures on Medicare, Medicaid and other health care insurance spending. These controls and limits could affect the payments we collect from sales of our products. Internationally, medical reimbursement systems vary significantly, with some medical centers having fixed budgets, regardless of levels of patient treatment, and other countries requiring application for, and approval of, government or third-party reimbursement. Even if we or our partners succeed in bringing transgenically produced products to market, uncertainties regarding future health care policy, legislation and regulation, as well as private market practices, could affect our ability to sell our products in commercially acceptable quantities at profitable prices.

The manufacture and sale of our products may expose us to product liability claims for which we could have substantial liability.

We face an inherent risk of product liability exposure related to testing of our transgenically produced products in human clinical trials and will face even greater risks when we commercialize our products. An individual may bring a product liability claim against us if one of our products causes, or is claimed to have caused, an injury or is found to be unsuitable for consumer use, even if the product involved is granted regulatory authorization for commercial sale. We have obtained product liability coverage for the clinical trials conducted to support the

filing for marketing approval of ATryn® with the FDA through our own policies. Product liability insurance for commercial sales of ATryn® has been established by OVATION. It is possible that our insurance coverage will not be sufficient to cover any claim. Any product liability claim brought against us, with or without merit, could result in:

- liabilities that substantially exceed our product liability insurance, which we would then be required to pay from other sources, if available;
- an increase of our product liability insurance rates or the inability to maintain insurance coverage in the future on acceptable terms or at all;
- damage to our reputation and the reputation of our products, resulting in lower sales;
- regulatory investigations that could require costly recalls or product modifications; and
- the diversion of management's attention from managing our business.

We may be unable to attract and retain qualified managerial and scientific personnel which could adversely affect our business and operations.

We are highly dependent on the principal members of our scientific and management staff. Our success will depend in part on our ability to identify, attract and retain qualified managerial and scientific personnel. There is intense competition for qualified personnel in our industry. We may not be able to continue to attract and retain personnel with the advanced technical qualifications or managerial expertise necessary for the development of our business. If we fail to attract and retain key personnel, it could have a material adverse effect on our business, financial condition and results of operations. We have employment agreements with our executive officers, but these agreements do not guarantee that they will remain employed with us in the future. If we lose an executive officer, or a significant number of our staff, or are unable to hire and retain qualified personnel, then our ability to develop and commercialize our products and processes may be delayed or impaired. We do not carry key personnel insurance.

Our ability to negotiate with potential marketing partners may be limited by existing obligations.

If we choose to commercialize ATryn® with an additional marketing partner outside of Asia, Genzyme Corporation has an exclusive first right of negotiation for commercialization rights. For any antithrombin product, this right is triggered on a product-by-product and market-by-market basis at such time as we make a submission to a regulatory authority for marketing approval in a given market. This right may delay our ability to negotiate a favorable agreement with a potential partner or distributor. This right does not apply if we have already entered into a collaboration or other agreement with a prospective research, development and exclusive marketing partner prior to such regulatory submission.

If we fail to maintain an effective system of internal controls, we may not be able to accurately report our financial results or prevent fraud. As a result, investors may lose confidence in our financial reporting.

The Sarbanes-Oxley Act of 2002 requires that we report annually on the effectiveness of our internal controls over financial reporting. Among other things, we must perform systems and process evaluation and testing. We must also conduct an assessment of our internal controls to allow management to report on our internal controls over financial reporting, as required by Section 404 of the Sarbanes-Oxley Act. These requirements were effective for the first time for 2004. In connection with our Section 404 compliance efforts, we have incurred or expended, and expect to continue to incur or expend, substantial accounting and other expenses and significant management time and resources. Any subsequent assessment by us or our independent registered public accounting firm may reveal significant deficiencies or material weaknesses in our internal controls, which may need to be disclosed in subsequent periodic reports filed with the Securities and Exchange Commission, or SEC, and could result in a restatement of previously issued financial information. Disclosures of this type could cause investors to lose confidence in our financial reporting and may negatively affect the price of our common

stock. Moreover, effective internal controls are necessary to produce reliable financial reports and to prevent fraud. If we have deficiencies in our internal controls over financial reporting, these deficiencies may negatively impact our business and operations.

RISKS RELATED TO OUR COMMON STOCK

Our common stock is at risk for delisting from the Nasdaq Global Market.

Our common stock is currently listed on the Nasdaq Capital Market, having moved from the Nasdaq Global Market in July 2008. Nasdaq has requirements that a company must meet in order to remain listed on the Nasdaq Capital Market. These requirements include maintaining a minimum closing bid price of $1.00 per share, which we have not maintained since February 2008. Our transfer to the Nasdaq Capital Market provided us with a 180-day period, or until January 12, 2009, to regain compliance with the minimum closing bid requirement for a minimum of 10 consecutive trading days. Based on Nasdaq's recent extension of the temporary suspension of Marketplace Rule 4450(a)(5), we have until at least July 20, 2009 to regain compliance with the minimum closing bid price requirement for a minimum of ten consecutive trading days. Although our non-compliance has no effect on the listing of our common stock at this time, there is no guarantee that we will be able to regain compliance with the minimum closing bid requirement. Additionally, Nasdaq may, in its discretion, require us to maintain a bid price of at least $1.00 per share for a period in excess of ten consecutive trading days before determining that we have demonstrated an ability to maintain long-term compliance.

At our annual meeting of stockholders in June 2008 our stockholders approved a proposal to grant our Board of Directors the discretionary authority to effect a reverse stock split of the issued and outstanding shares of our common stock at any time prior to our 2009 Annual Meeting of stockholders. The primary purpose for effecting a reverse stock split would be to increase the per share price of our common stock in order to help us maintain the listing of our common stock on the Nasdaq Capital Market. However, even if a reverse stock split is effected, an increase in the per share price of our common stock above $1.00 may not be able to be maintained. The market price of our common stock will continue to be based, in part, on our performance and other factors unrelated to the number of shares outstanding.

If we do not regain compliance with the minimum bid price requirement by July 20, 2009, Nasdaq will provide us written notification that our common stock is subject to delisting. If we have not achieved compliance by that date, we may appeal Nasdaq's determination to delist our common stock to the Nasdaq Hearing Panel, but there is no guarantee that such an appeal would be successful.

In November 2008, we received notice from the Listing Qualifications Staff of the Nasdaq Stock Market indicating that we no longer satisfied the minimum stockholders' equity requirement for continued listing on the Nasdaq Capital Market under Nasdaq Marketplace Rule 4310(c)(3). We subsequently submitted to the Nasdaq staff, a plan to regain compliance, and the Nasdaq, in response to the compliance plan submitted, granted us an extension to February 19, 2009 to regain compliance. On January 21, 2009, we received notice from the Staff indicating that we had regained compliance by exceeding $35 million of market capitalization for 10 consecutive trading days. Even though we have regained compliance with Nasdaq Marketplace Rule 4310(c)(3), there is no guarantee that we will be able to maintain compliance over future periods.

If we fail to meet the continued listing requirements of the Nasdaq Capital Market and our common stock is delisted, trading in our common stock, if any, could be conducted on the OTC Bulletin Board as long as we continue to file reports required by the Securities and Exchange Commission. The OTC Bulletin Board is generally considered to be a less efficient market than the Nasdaq Capital Market, and our stock price, as well as the liquidity of our common stock, would be adversely affected as a result. Delisting would also negatively impact our ability to sell our common stock and secure additional financing.

We have obligations to issue shares of common stock in the future that will dilute your ownership interest.

As of December 28, 2008, in addition to approximately 103 million shares of our common stock outstanding, there were:

(i) warrants outstanding to purchase an aggregate of approximately 43.7 million shares of our common stock at exercise prices ranging from $0.31 to $6.30 per share, which were issued to investors in various prior financings;

(ii) an outstanding convertible note to LFB that is convertible after June 1, 2009 into 48.4 million shares of our common stock; and

(iii) options to purchase an aggregate of 8.8 million shares of common stock at varying exercise prices were outstanding, of which total, options to purchase 4.4 million shares were immediately exercisable and the underlying shares could be immediately resold into the public market.

The warrants to purchase an aggregate of 1,828,573 of shares of our common stock, which we issued in our August 2005 private placement, had an initial exercise price of $2.68 per share. The exercise price of these warrants is subject to adjustment upon the occurrence of a dilutive issuance, that is, an issuance of any shares of our common stock or common stock equivalents at an exercise price lower than the then-effective exercise price per share. Upon a dilutive issuance the exercise price of the unexercised portion of these warrants shall be reduced by multiplying the then-effective exercise price by a fraction, the numerator of which is the number of shares of common stock outstanding immediately prior to the dilutive issuance plus the number of shares of common stock which the aggregate consideration received or deemed to be received by the company in connection with the dilutive issuance would purchase at the exercise price, and the denominator of which is the number of shares of common stock and common stock equivalents issued and outstanding immediately following such dilutive issuance. As adjusted for all dilutive issuances through December 22, 2008, the exercise price of the August 2005 warrants has been reduced to approximately $1.34 per share.

We have 115 shares of Series D convertible preferred stock outstanding as of December 28, 2008, which are convertible into a total of 115,000 shares of common stock at the option of the preferred stock holder, LFB, at any time.

We also have a convertible note payable to LFB in the remaining amount of approximately $800,000 as of December 28, 2008, the principal and accrued interest of which automatically converts into shares of our common stock in conjunction with any future common stock offerings at the per share offering price of the respective offering.

Our capital raising efforts will dilute shareholder interests.

If we raise additional capital by issuing equity securities, the issuance will result in a reduction of the percentage of ownership for our existing shareholders, a result commonly referred to as dilution. The extent of such dilution will vary based upon the amount of capital raised.

Our common stock may continue to have a volatile public trading price.

Historically, the market price of our common stock has been highly volatile and the market for our common stock has experienced significant price and volume fluctuations, some of which are unrelated to our company's operating performance. Since January 1, 2007, the trading price of our stock has fluctuated from a high of $1.25 to a low of $0.11. It is likely that the market price of our common stock will continue to fluctuate in the future. Factors which may have a significant adverse effect on our common stock's market price include:

- actual or potential clinical or regulatory events relating to our products or compounds under development;
- sales of substantial amounts of our common stock in the public market, or the perception that such sales may occur;

- other regulatory developments in Europe or the United States;
- announcements by us or our competitors of technological innovations or new commercial products;
- an unexpected termination of one of our partnerships;
- developments concerning our proprietary rights, including patent and litigation matters;
- general market conditions; and
- quarterly fluctuations in our cash position, revenues and other financial results.

The reported average daily trading volume of our common stock for the twelve-month period ending December 28, 2008 was 275,054 shares.

Anti-takeover provisions in our charter and by-laws and Massachusetts law may result in management entrenchment and adversely affect our stock price.

Anti-takeover provisions in our charter, our by-laws and Massachusetts statutes could delay or make more difficult a merger, tender offer or proxy contest involving us. These provisions may delay or prevent a change of control without action by the shareholders, and may resist important changes shareholders seek to make if they are dissatisfied with the conduct of our management. Therefore, these provisions could result in the entrenchment of our management and adversely affect the price of our common stock.

Our charter grants authority to the board of directors to issue series of preferred stock with certain rights and privileges, including voting rights, as it deems appropriate. This authority may enable our board of directors to deter or delay a change in control despite a shift in stock ownership, as a result of an increase in the number of shares needed to gain voting control. This may have the effect of discouraging tender offers and proxy contests, and give management the power to reject certain transactions which might be desired by shareholders. This provision could also be deemed to benefit incumbent management to the extent it deters offers by persons who would wish to make changes in management or exercise control over management.

In addition, our by-laws may have the effect of preventing changes in our management because shareholders are required to give us written notice of any proposal or director nomination within a specified period of time before the annual meeting of shareholders, certain qualifications for a person to be elected to the board of directors must be established, and shareholders are prohibited from calling a special meeting of shareholders, unless the shareholder owns 90% of our outstanding voting stock.

Our shareholder rights plan is another anti-takeover device. It involves a distribution to our shareholders of certain rights to acquire shares of our capital stock in the event of an acquisition of a predetermined number of shares by an investor. The shareholder rights plan is designed to deter coercive takeover tactics and to encourage a party interested in acquiring the corporation to negotiate with the board of directors.

Certain Massachusetts corporate statutes provide anti-takeover protections. Our charter gives effect to a provision of Massachusetts law that places directors of publicly-held Massachusetts corporations into three classes of nearly equal sizes with staggered terms, thereby permitting only one-third of the board of directors to be elected at once. In addition, with certain exceptions, Massachusetts law prohibits a publicly-held Massachusetts corporation from engaging in a business combination transaction with an "interested stockholder" for a period of three years. An "interested stockholder" is a person who owns 5% or more of the outstanding voting stock of the corporation. Finally, our by-laws include a provision excluding us from the applicability of a Massachusetts statute that denies voting rights to any person acquiring 20% or more of the outstanding voting stock of a corporation, unless such voting rights are approved by a majority of the corporation's disinterested shareholders. Our by-laws may be amended at any time to subject us to this statute prospectively.

LFB, the stockholder with the largest beneficial ownership of our common stock, may seek to influence our business in a manner that is adverse to us or adverse to other stockholders who may be unable to prevent actions by LFB.

As our largest stockholder, LFB has substantial control over the outcome of most actions requiring the approval of our stockholders. After June 1, 2009, if we have not paid off the $15 million convertible debt we owe to LFB, the debt becomes convertible into 48,387,096 shares or our common stock and, if it is converted and LFB fully exercises the warrant issued to it in the debt financing for an aggregate of 23,193,548 shares of our common stock, LFB would own 91,844,048 shares, or 52.6%, of our common stock and would be in a position to control the election of our directors. We cannot assure that LFB will not seek to influence our business in a manner that is contrary to our goals or strategies or the interests of other stockholders. Moreover, persons who are directors of GTC and who are also directors and/or officers of LFB may decline to take action in a manner that might be favorable to us but adverse to LFB.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

All of our facilities are located in Massachusetts. We own a 383-acre facility in central Massachusetts. This facility contains 106,793 square feet of production, laboratory and administrative space and currently houses more than 1,500 goats. This facility is subject to a mortgage in favor of General Electric Capital Corporation and a second mortgage in favor of LFB Biotechnologies. We lease approximately 32,356 square feet of office and laboratory space which expires in September 2010. In February 2007, we signed a lease amendment to lease an additional 8,188 square feet of office space which also expires in September 2010.

We believe that our owned and leased facilities are adequate for significant further development of commercial transgenic products.

ITEM 3. LEGAL PROCEEDINGS

LEO Pharma informed us in September 2008 of their internal reprioritization and desire to transfer the ATryn® program to us or a third party. LEO has attempted to terminate its 2005 collaboration agreement with us for alleged cause before completion of the Phase II study in DIC. However, LEO has made it clear to us that their decision was not based on any safety or efficacy issues. We do not believe that LEO has any basis for such termination, and we further believe that LEO is in breach of the agreement. We initiated International Chamber of Commerce (ICC) arbitration proceedings in the fourth quarter of 2008. We have asked the tribunal to determine that LEO is obligated to perform the agreement, including completion of the Phase II study, and is not legally entitled to exercise its contractual remedies on termination for alleged cause, or alternatively that we are entitled to damages with respect to LEO's actions. While we have sought to conclude this matter by reaching agreements with LEO and a new partner for the collaboration to transfer the DIC trial to the new partner, we believe we are taking necessary and appropriate steps to protect our legal rights through the arbitration process. This process is still in the preliminary stages, and we cannot predict its likely outcome or, in the event of an unfavorable outcome, the potential consequences to us, including cost.

BioProtein Technologies Company, a French corporation, brought a legal action against LFB and GTC in France on a breach of contract claim regarding a contract between BioProtein and LFB. LFB is the principal defendant, but we were joined in the lawsuit based on the allegations by BioProtein that we tortiously interfered with an existing contract between LFB and BioProtein. The total claim against both parties is for 31 million euros. We have retained counsel in France and we will vigorously defend ourselves. However, pursuant to our Joint Commercialization and Development Agreement with LFB, LFB has agreed to fully indemnify us with respect to any legal fees and damages arising from this lawsuit.

We are not party to any other material pending legal proceedings, other than ordinary routine litigation incidental to our business.

ITEM 4. SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS

We held a Special Meeting of Stockholders on December 10, 2008. The following represents the results of voting on the proposals submitted to the Company's stockholders:

(1) Proposal to approve the issuance of a secured note convertible into shares of our common stock and warrant to purchase shares of our common stock to LFB Biotechnologies S.A.S.U. pursuant to the Note and Warrant Purchase Agreement dated as of October 31, 2008 between us and LFB:

Total Vote "FOR"	Total Vote "AGAINST"	Total Vote Abstaining	Total Broker Non-Votes
54,021,740	6,713,794	412,553	26,409,750

(2) Proposal to approve an amendment to our 2002 Equity Incentive Plan (the "2002 Plan") to increase by 2,000,000 shares the number of shares of common stock available for issuance under the 2002 Plan and amend the annual adjustment provision under the 2002 Plan:

Total Vote "FOR"	Total Vote "AGAINST"	Total Vote Abstaining	Total Broker Non-Votes
52,905,881	7,708,542	533,664	26,409,750

(3) Proposal to approve an amendment to our restated Articles of Organization, as amended, to increase by 10,000,000 shares of the number of authorized shares of our common stock to 210,000,000 shares:

Total Vote "FOR"	Total Vote "AGAINST"	Total Vote Abstaining	Total Broker Non-Votes
76,072,553	10,378,925	1,106,359	—

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Our Common Stock was traded on the Nasdaq Global Market under the symbol GTCB until July 2008 when we transferred our listing to the Nasdaq Capital Market under the same symbol. Quarterly high and low sales prices for the Common Stock as reported by the Nasdaq Global Market and the Nasdaq Capital Market for those respective periods are shown below:

2007:		
1st Quarter (ended April 1)	$ 1.21	$ 0.96
2nd Quarter (ended July 1)	1.25	1.03
3rd Quarter (ended September 30)	1.23	0.98
4th Quarter (ended December 30)	1.12	0.84
2008:		
1st Quarter (ended March 30)	$ 1.19	$ 0.45
2nd Quarter (ended June 29)	0.73	0.36
3rd Quarter (ended September 28)	0.76	0.28
4th Quarter (ended December 28)	0.42	0.11

On February 20, 2009, the closing price of our Common Stock was $0.35 per share as reported on the Nasdaq Capital Market.

As of February 20, 2009, we had approximately 1,321 shareholders of record.

We have never paid a cash dividend on our Common Stock and do not expect to do so for the foreseeable future.

ITEM 6. SELECTED FINANCIAL DATA

The selected financial data set forth below as of December 28, 2008 and December 30, 2007 and for each of the three fiscal years in the period ended December 28, 2008 are derived from our consolidated financial statements included elsewhere in this Report, which have been audited by PricewaterhouseCoopers LLP, an independent registered public accounting firm. The report of PricewaterhouseCoopers LLP included in this report contains an explanatory paragraph relating to our ability to continue as a going concern, as described in Note 1 to the consolidated financial statements. The selected financial data set forth below as of December 31, 2006, January 1, 2006 and January 2, 2005 and for the years ended January 1, 2006 and January 2, 2005 are derived from audited consolidated financial statements not included in this Report.

This data should be read in conjunction with the Section entitled "Management's Discussion and Analysis of Financial Condition and Results of Operations" under Item 7 of this Annual Report and our consolidated financial statements and related notes thereto under Item 8 of this Annual Report.

SELECTED FINANCIAL DATA
(Dollars in thousands except per share data)

	December 28, 2008	December 30, 2007	December 31, 2006	January 1, 2006	January 2, 2005
Statement of Operations Data:					
Revenue	$ 16,656	$ 13,896	$ 6,128	$ 4,152	$ 6,626
Costs of revenue and operating expenses:					
Cost of revenue	8,624	11,561	6,651	4,344	6,107
Research and development	21,031	28,925	25,401	21,145	20,002
Selling, general and administrative	10,208	9,834	9,723	8,428	9,710
	39,863	50,320	41,775	33,917	35,819
Operating loss from continuing operations	(23,207)	(36,424)	(35,647)	(29,765)	(29,193)
Other income and (expenses):					
Interest income	184	1,443	1,237	547	312
Interest expense	(1,183)	(1,329)	(1,001)	(1,140)	(951)
Other income (expense)	1,541	(11)	66	246	339
Net loss	(22,665)	(36,321)	(35,345)	(30,112)	(29,493)
Net loss per common share (basic and diluted)	$ (0.23)	$ (0.47)	$ (0.53)	$ (0.62)	$ (0.79)
Weighted average number of shares outstanding (basic and diluted)	98,199,691	77,863,008	66,860,345	48,658,143	37,360,758

	December 28, 2008	December 30, 2007	December 31, 2006	January 1, 2006	January 2, 2005
Balance Sheet Data:					
Cash, cash equivalents and marketable securities	$ 11,643	$ 15,765	$ 43,385	$ 36,169	$ 22,281
Working capital	(2,302)	(1,740)	29,382	18,601	10,639
Total assets	40,403	40,713	73,235	66,719	57,301
Long-term liabilities	28,469	13,970	16,443	9,688	9,336
Shareholders' equity	(4,123)	8,024	37,956	36,709	33,653

There were no cash dividends paid to common shareholders for any period presented.

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

Overview

We are the leader in the development and production of human therapeutic proteins through transgenic technology that enables animals to produce what is known as a recombinant form of a specified human protein in their milk. Using this technology, we are developing a portfolio of recombinant blood proteins to treat a range of genetic and acquired blood deficiencies, including hemophilia and other blood coagulation disorders. These blood proteins, also known as plasma proteins, are difficult to produce in other manufacturing systems, and some are currently only available by extraction from human blood. We have also initiated the development of a portfolio of monoclonal antibodies, or MAbs, for use as potential follow-on biologics targeted at several large market products. The level and speed of development of our proprietary products will be dependent upon our financial resources and new partnering arrangements as well as progress made in the legislative process as related to follow-on biologics. After ATryn®, the next highest priority is rhFVIIa.

Our first product ATryn®, is a recombinant form of human antithrombin, a blood protein with anticoagulation and anti-inflammatory properties. In 2006, ATryn® became the first transgenically produced therapeutic protein to be approved anywhere in the world when we obtained European Commission approval of the use of ATryn® as a prophylactic treatment for patients with hereditary antithrombin deficiency, or HD, undergoing surgical procedures. On February 6, 2009, we received United States Food and Drug Administration, or FDA, approval for ATryn® for HD patients undergoing surgery or childbirth in the United States, making ATryn® the first transgenically derived therapeutic protein approved by the FDA. The FDA has also designated ATryn® an Orphan Drug in this indication. Along with the approval of ATryn®, the FDA's Center for Veterinary Medicine also approved our New Animal Drug Application, the first of its kind to regulate genetically engineered animals. This is now required for a recombinant technology used to develop transgenic animals, such as the goats that produce recombinant antithrombin. We believe that the regulatory approval of ATryn® in Europe and the U.S. achieved an important validation of our production technology, which will assist in obtaining approvals for other compounds and in other countries.

We plan to develop our portfolio of recombinant proteins through strategic collaborations:

- In June 2008, we entered into a collaboration agreement with OVATION Pharmaceuticals to develop and market ATryn® in the United States. The collaboration agreement includes the commercialization of ATryn® in the HD indication and the further development of ATryn® in acquired antithrombin deficiency indications, or AD.
- In September 2006, we entered into a collaboration agreement with LFB Biotechnologies, or LFB, to develop selected recombinant plasma proteins and MAbs. The first program in this collaboration is for the development of a recombinant form of human blood coagulation factor VIIa for the treatment of patients with hemophilia. This collaboration has now been established in a separate joint venture entity, and we have added to the joint venture programs to develop a recombinant form of human blood coagulation factor IX, recombinant human alpha-1 antitrypsin, as well as an antibody to the CD20 immune system receptor, the same target as for the MAb marketed as Rituxan®.

We have also used our transgenic technology in external programs to produce therapeutic products for our partners. For our external programs, we enter into licensing and development agreements with partners to use our transgenic technology to develop, produce and purify recombinant forms of therapeutic proteins. Historically, we operated on a service contract basis, generally receiving fees for the development of the production platform and production and purification of the proteins. As of December 28, 2008, we have one active external program with PharmAthene. Most of our fiscal 2008 revenues were derived from our external programs.

We have operated at a net loss since our inception in 1993, and we used $19.7 million of cash in operating cash flows in 2008. We are entirely dependent upon funding from equity financings, partnering programs and proceeds from short and long-term debt to finance our operations until we achieve commercial success

in selling and licensing our products and positive cash flow from operations. Based on our cash balance as of December 28, 2008, as well as potential cash receipts from existing programs, we believe our resources will be sufficient to fund operations into the second quarter of 2009. We expect that future sources of funding may include new or expanded collaboration arrangements and sales of equity or debt securities. If no funds are available, we would have to sell or liquidate the business. If adequate funds are not available, we may be required to delay, reduce the scope of or eliminate our research and development programs, obtain funds through arrangements with collaborators or others that may require us to relinquish rights to certain product candidates that we might otherwise seek to develop or commercialize independently. Additionally, any future equity funding may dilute ownership of our existing equity investors.

Our key value drivers include the following:

ATryn®

We have a collaboration agreement with OVATION to develop and market ATryn® in the United States. The collaboration agreement includes the commercialization of ATryn® in the HD indication and the further development of ATryn® in AD indications. The milestone payments to us under this agreement include a total of $9 million through approval of ATryn® for HD in the U.S., $5 million of which was received in 2008 and $4 million is expected to be received in the first quarter of 2009. The collaboration anticipates further development of ATryn® in larger market acquired deficiencies such as the treatment of heparin resistance in patients undergoing cardiopulmonary bypass surgery and the treatment of DIC associated with severe sepsis.

Under our agreement with OVATION, we are developing ATryn® for the treatment of heparin resistance in patients undergoing coronary artery bypass graft (CABG) surgery that requires the use of a cardio pulmonary bypass (CPB) machine. Patients undergoing this surgery require anticoagulation with heparin to prevent clotting, which can occur when blood comes into contact with the tubing of the CPB machine performing the heart's function during surgery. Patients with heparin resistance generally do not respond adequately to the dose of heparin normally required to achieve sufficient anticoagulation for them to go on to the CPB machine. The overall incidence of heparin resistance has been reported to range from 10% to over 22% of CABG patients. Treatment of heparin resistant patients with fresh frozen plasma, which contains low concentrations of antithrombin, is one option to restore heparin sensitivity and achieve adequate anticoagulation to permit initiation of CPB. We previously completed two Phase III studies in the heparin resistance indication, and we are planning to conduct one additional Phase III study to determine the safety and efficacy of ATryn® in restoring heparin sensitivity in heparin resistant CABG patients as a basis for marketing approval in this indication.

We also have a collaboration agreement with LEO Pharma A/S, or LEO, for the commercialization of ATryn® in HD in Europe, Canada, and the Middle East and for its further development in AD indications. LEO selected DIC associated with severe sepsis as the first AD indication in which to conduct additional clinical studies under this collaboration. In DIC, the septic infection consumes the patient's native antithrombin faster than the body can replace it, leading to clotting and inflammation problems that can cause death. Of the approximately 220,000 patients in the European Union and 250,000 patients in the U.S. with DIC in severe sepsis annually, approximately 50% die from the condition. We estimate that the annual market potential for DIC in the U.S. alone is $2 - 3 billion.

LEO initiated a Phase II dose-ranging study in the DIC indication in 2007. In the third quarter of 2008, LEO advised us that, as a result of an internal re-assessment of their strategic priorities, they wished to enter into negotiations to transfer the ATryn® program to us or an alternate partner. Pending any such transfer, further patients are not being enrolled in the study at this time. LEO has made it clear to us that their decision was not based on any safety or efficacy issues. We are currently engaged in a dispute resolution process with LEO, as described under Item 3 in this Annual Report.

LFB Collaboration Agreement

Under our collaboration agreement with LFB for the development of selected recombinant plasma proteins we now have four ongoing programs. In 2008, we amended our agreement with LFB to establish LFB/GTC LLC, a separate legal entity for the joint venture. This amendment added LFB/GTC LLC as a party to the agreement and provided that rights to the intellectual property of the new joint venture will flow through this entity. This amendment also reflected LFB's agreement to provide up to $6 million in funding for our 2008 development costs related to the programs under the LFB collaboration. All other terms and conditions remain the same.

Under this joint venture, we are to share equally with LFB in the cost of the development and commercialization of each product and we will be entitled to 50% of any profits derived from products developed through the joint venture, provided we each contribute equally to the costs of their development. In the event that contributions to the development are not equal, the profit allocation will be adjusted based on development costs incurred. Through 2008, LFB has contributed 85% of the costs of the joint venture and owns the same percentage of future profits, subject to our right to reestablish our 50% ownership by repaying LFB our share of costs plus a specified premium that increases over time as clinical development progresses. Under the agreement, a joint steering committee of each company's representatives determines product development and commercialization plans. Our activities under this program in 2008 were primarily focused on development of the production and purification system. We anticipate that the rhFVIIa product will enter clinical studies in 2010 to evaluate its use in treating hemophiliacs that have developed inhibitors to coagulation factors VIII or IX. During 2008, we received approximately $5.6 million in funding from LFB, of which $5.1 million was recorded against the program costs in research and development for our actual costs incurred during 2008, the remaining $500,000 was recorded as a payable to the joint venture. During 2007, we received approximately $1.2 million in funding from LFB as reimbursement for an agreed portion of our costs incurred in these programs which was recorded against the program costs in research and development.

For a detailed discussion of the programs that are included in the joint venture, see Item 1 of this Annual Report.

External Program Portfolio

We believe the advantages to external partners of using our transgenic production technology include enabling the development of proteins that are difficult to produce in traditional recombinant production systems, requiring significantly lower capital investment, assuring lower cost of goods, and providing for flexibility in capacity expansion. To date we have typically developed a transgenically produced version of an external partner's protein on a service contract basis. We are in the process of transitioning that model into a portfolio of programs where we obtain benefits beyond the margin of a service contract, such as fees for successful downstream partnering with third parties, royalties, or some other relationship with the partner beyond fees or milestones collected for development of the production platform.

Critical Accounting Policies and Estimates

The preparation of consolidated financial statements requires that we make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses, and related disclosure of contingent assets and liabilities. Our critical accounting policies are summarized in Note 2 in the Notes to Consolidated Financial Statements included in Item 8 of this Annual Report. On an on-going basis, we evaluate our estimates, including those related to revenue recognition, investments, intangible and long-lived assets, income taxes, accrued expenses, financing operations, and contingencies and litigation. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Our actual results may differ from these estimates under different assumptions or conditions.

We believe that our application of the following accounting policies involve the most significant judgments and estimates used in the preparation of our consolidated financial statements.

Revenue Recognition

We enter into licensing and development agreements with collaborative partners for the development, production and purification of our internally developed recombinant protein candidates or for a transgenically produced version of the partner's therapeutic recombinant proteins. The terms of the agreements typically include non-refundable license fees, funding of research and development, transfer price payments for manufactured material, payments based upon the achievement of certain milestones and royalties on future product sales, if any.

We recognize revenue in accordance with Staff Accounting Bulletin No. 101, "Revenue Recognition in Financial Statements" (SAB No. 101), as amended by Staff Accounting Bulletin No. 104, "Revenue Recognition" (SAB No. 104), and Emerging Issues Task Force Issue No. 00-21, "Revenue Agreements with Multiple Deliverables" (EITF No. 00-21).

Revenues from the sale of products and services are recognized when persuasive evidence of an agreement exists, delivery has occurred or services have been rendered, the fees are fixed and determinable, and collectibility is reasonably assured. Revenues from royalties on third-party sales of licensed technologies will be generally recognized in accordance with the contract terms when the royalties can be reliably determined and collectibility is reasonably assured.

We assess multiple element revenue arrangements involving upfront payments, license fees, manufacturing services and milestone payments received for the delivery of rights or services. The following criteria must be met for an element to represent a separate unit of accounting:

a) The delivered items have value to a customer on a standalone basis;

b) There is objective and reliable evidence of the fair value of the undelivered items; and

c) Delivery or performance is probable and within our control for any delivered items that have a right of return.

If these criteria are met, we apply the appropriate revenue recognition model as described above to each separate unit of accounting. If these criteria are not met, elements are combined into a single unit of accounting and revenue is not recognized until we have verifiable objective evidence of the undelivered element. Upfront payments and license fees are recognized ratably over the longer of the contractual term or expected relationship period. Payments for the achievement of substantive milestones are recognized when the milestone is achieved. Payments for milestones which are not the result of the achievement of a substantive milestone, are recognized ratably over the longer of the remaining contractual term or expected relationship period.

Revenue is also recognized in accordance with SAB 101 FAQ 13 (EITF 91-6). Under that model, revenue is recognized using the lesser of non-refundable cash received and milestones met or the result achieved using level-of-efforts accounting. The estimated costs to complete each program are based on the contract terms, detailed program plans, including cost projections, and each program under review. All revenue recognition estimates are made based upon the current facts and circumstances and are reassessed on at least a quarterly basis. There are a number of factors which could cause the need for a revision to these estimates, which in turn may have the effect of increasing or decreasing revenue in the current period as they become known. These factors include unforeseen additional costs, delay in a program, efficiencies or decisions at the partner's discretion.

The following table summarizes our revenues by customer / partner as a percent of revenue in the last three years:

	2008	2007	2006
Merrimack	23%	29%	54%
LEO	27%	32%	32%
PharmAthene	39%	28%	—
Other	11%	11%	14%
	100%	100%	100%

Deferred revenue arises from payments received in advance of the culmination of the earnings process. Deferred revenue expected to be recognized within the next twelve months is classified as a current liability. Deferred revenue will be recognized as revenue in future periods when the applicable revenue recognition criteria have been met.

Inventory

All of our inventory on hand as of December 28, 2008 and December 30, 2007 related to ATryn®. The net book value of this inventory as of December 30, 2007 was zero because our estimated cost to complete then pending orders for LEO exceeded the agreed upon maximum transfer price. Currently, because we have only two customers, we only capitalize inventory if orders have been received. Any inventory that we may capitalize in the future will be based on our expectation that it will be sold for clinical trials and commercial sale. If at any time we believe that the sale of inventory is no longer probable, we will charge the inventory to expense.

We analyze our inventory levels and estimate demand for commercial sale and clinical trials on a quarterly basis based on orders received. The assessment of the expected use of the inventory is highly judgmental and is based on our best estimate for demand related to both commercial sale and clinical trial usage. We also review the appropriate carrying value of the inventory based on the estimated selling price of the material taking into account inventory obsolescence and inventory expiration dates. We project our current cost of production to exceed the agreed upon maximum transfer price for clinical studies until we reach larger production volumes, and we will expense all costs above the agreed upon maximum transfer price.

Valuation of Intangible and Long-Lived Assets

Management's policy regarding long-lived assets is to evaluate the recoverability of our assets when the facts and circumstances suggest that these assets may be impaired. This analysis relies on a number of factors, including operating results, business plans, budgets, economic projections and changes in management's strategic direction or market emphasis. The test of such recoverability is a comparison of the asset value to its expected cumulative undiscounted net operating cash flow over the remaining life of the asset. If an impairment exists it is measured by the excess of the carrying value over the discounted cash flows. Any write-downs are to be treated as permanent reductions in the carrying amount of the assets.

Share-Based Compensation

Effective January 2, 2006, we adopted SFAS 123(R) Share-Based Payment (or SFAF 123(R)), which requires companies to measure and recognize compensation expense for all share-based payments at fair value.

Under the modified prospective approach, SFAS 123(R) applies to new awards and to awards that were outstanding on January 2, 2006. Under the modified prospective approach, compensation expense recognized during fiscal 2006 includes compensation expense for all share-based payments granted prior to, but not yet vested on, January 2, 2006, based on the grant-date fair value estimated in accordance with the provisions of SFAS 123(R), and compensation expense for all share-based payments granted subsequent to January 2, 2006, based on the grant-date fair value estimated in accordance with the provisions of SFAS 123(R). Prior periods were not restated to reflect the impact of adopting the new standard.

Changes in the inputs and assumptions can materially affect the measure of the estimated fair value of our employee equity awards. Also, the accounting estimate of share-based compensation expense is reasonably likely to change from period to period as further equity awards are granted and adjustments are made for equity award forfeitures and cancellations.

Included within the statements of operations are the following charges for share-based compensation, which includes both options and restricted stock units:

	(dollars in thousands)		
	December 28, 2008	December 30, 2007	December 31, 2006
Research and development expense	$ 293	$ 359	$ 312
Selling, general and administrative expense	367	488	254
Total share-based compensation	$ 660	$ 847	$ 566

Results of Operations

The key components to our losses are revenue, cost of revenue, research and development expenses, and selling, general and administrative expenses.

2008 as Compared to 2007

	($ in thousands)			
	2008	2007	$ Change	% Change
Revenue	$ 16,656	$ 13,896	$ 2,760	20%
Cost of revenue	$ 8,624	$ 11,561	$ (2,937)	(25)%
Research and development	$ 21,031	$ 28,925	$ (7,894)	(27)%
Selling, general and administrative	$ 10,208	$ 9,834	$ 374	4%
Other income	$ 542	$ 103	$ 439	426%

Revenue. During 2008, we derived approximately $11.6 million of revenue from our external development programs, of which $6.6 million related to our work with PharmAthene, $3.8 million related to the Merrimack program, which was completed in the third quarter of 2008, $4.2 million from sales to LEO as well as $626,000 from the CD137 program. During 2007, we derived $9 million of our revenue from external programs, primarily with Merrimack and PharmAthene, as a result of the timing of milestones met on the programs during 2007, and $4.2 million from sales to LEO. We expect revenue from external programs and product shipments relating to ATryn® to continue to vary due to the nature, timing and specific requirements for these development activities.

Cost of revenue. The decrease in cost of revenue was primarily the result of inventory write-offs that resulted in higher costs in 2007, including a $2.9 million write-off of ATryn® inventory which was rendered unusable as a result of the fill/finish process conducted at a U.S. based third party fill/finish contractor and a write-off of $469,000 during 2007 of in-process inventory which was determined not to meet specifications during release testing for commercial use. In 2008, we received $1.5 million from the contractor for settlement of this loss which was recorded to other income. These decreases were partially offset by a net increase in costs on our external programs due to the stage of development of those programs. Even excluding the impact of these write-offs, the level of expenses for our external programs will fluctuate from period to period depending upon the stage of development of individual programs as they progress.

Research and development expense. The 2008 research and development expense included $15.5 million related to the Atryn® program, a decrease of $5.5 million over the $21 million in 2007. Details of expenses for the ATryn® program for the respective years are as follows:

	($ in thousands)	
	2008	2007
ATryn® manufacturing expenses	$ 8,546	$ 12,401
EMEA regulatory process expenses	1,040	2,708
U.S. clinical trial expenses	5,247	5,091
Other	686	777
Total	$ 15,519	$ 20,977

Manufacturing costs included costs of producing clinical material in excess of the maximum transfer price to LEO as well as process development and validation costs for scale up of the ATryn® manufacturing process and costs associated with establishment of a second fill site.

During 2008 we incurred approximately $5.1 million of expense related to the programs under the LFB joint venture (rhFVIIa-$2.2M; CD20-$1.3M; rhFIX-$851,000; rhAAT-$795,000) and we received approximately $5.6 million of funding from LFB, of which approximately $500,000 was recorded as a payable to the joint venture at the end of 2008. During 2007 we incurred approximately $3.9 million related to the programs under the LFB collaboration (FVIIa $3.3 million, FIX $600,000; CD20 $70,000) and we received approximately $1.2 million in funding from LFB in 2007 as reimbursement for an agreed upon portion of our costs incurred in these programs.

We cannot estimate the costs to complete our ongoing research and development programs due to significant variability in clinical trial costs, the regulatory approval process and the stage of development.

Selling, General and Administrative Expense. The increase in SG&A expenses was primarily a result increased legal costs related to patents and partnering and financing transactions.

Other Income. The increase in other income was primarily a result of $1.5 million received and recorded in 2008 from the settlement of arbitration related to the write-off of ATryn® inventory that was rendered unusable as a result of the fill/finish process conducted at a U.S. based third party fill/finish contractor during 2007, partially offset by lower interest income based on our cash balance and interest expense.

2007 as Compared to 2006

	($ in thousands)			
	2007	2006	$ Change	% Change
Revenue	$ 13,896	$ 6,128	$ 7,768	127%
Cost of revenue	$ 11,561	$ 6,651	$ 4,910	74%
Research and development	$ 28,925	$ 25,401	$ 3,524	14%
Selling, general and administrative	$ 9,834	$ 9,723	$ 111	1%

Revenue. During 2007, we derived $9 million of our revenue from external programs, primarily with Merrimack and PharmAthene, as a result of the timing of milestones met on the programs during 2007, and $4.2 million from sales to LEO. During 2006, we derived $4 million of our revenue from external programs, primarily with Merrimack, as a result of the timing of milestones met on the program during 2006, and $2 million from sales to LEO. We expect revenues to continue to vary on a year-to-year basis.

Cost of revenue. The increase in cost of revenue was primarily the result of a $3 million increase in cost of goods sold associated with the sale of ATryn® product to LEO as compared to 2006, as well as a $2.9 million write-off of ATryn® inventory which was rendered unusable during the second quarter 2007 as a result of the fill/finish process conducted at a U.S. based third party fill/finish contractor and a write-off of $469,000 of in-process inventory which was determined not to meet specifications during release testing for commercial use. These increases were partially offset by a net reduction in costs on our external programs due to the stage

of development of those programs. Even excluding the impact of these write-offs, the level of expenses for our external programs will fluctuate from period to period depending upon the stage of development of individual programs as they progress.

Research and development expense. The 2007 research and development expense included $21 million related to the ATryn® program, an increase of $200,000 over the $20.3 million in 2006. Details of expenses for the ATryn® program for the respective years are as follows:

	(dollars in millions)	
	2007	2006
ATryn® manufacturing expenses	$ 12.4	$ 11.6
EMEA regulatory process expenses	2.7	3.4
U.S. clinical trial expenses	5.1	3.8
Write-down of prior year inventory	—	1.3
Other	0.8	0.2
Total	$ 21.0	$ 20.3

Manufacturing costs included costs of producing clinical material in excess of the maximum transfer price to LEO as well as process development and validation costs for scale up of the ATryn® manufacturing process and costs associated with establishment of a second fill site.

During 2007, we also incurred approximately $3.9 million of expense in support of the programs in our LFB collaboration (rhFVII-$3.3 million, rhFIX-$600,000; CD20-$70,000), which were partially offset by approximately $1.2 million in funding from LFB in 2007 as reimbursement for an agreed portion of our costs incurred in these programs. During 2006, we incurred approximately $200,000 of expense in support of the programs in our LFB collaboration.

Selling, General and Administrative Expense. The increase in SG&A expenses was primarily a result of increased costs related to FAS 123R expense of approximately $160,000, and increased legal costs related to patents and partnering and financing transactions of approximately $98,000 as well as costs of approximately $463,000 related to senior management hires, which were partially offset by lower professional fees and director and officer insurance. Our 2006 SG&A expenses included $225,000 related to the settlement of the litigation (see Note 5 to the Notes to Consolidated Financial Statements included in Item 8 of this Annual Report).

Liquidity and Capital Resources

Overview

Our objective is to finance our business appropriately through a mix of equity financings, partnering payments, receipts from contracts for external programs, grant proceeds, debt financings and interest income earned on our cash and cash equivalents, until such time as product sales and royalties occur and we achieve positive cash flow from operations. We expect that our ability to raise future funds will be affected by our ability to enter into new or expanded partnering arrangements or contracts for external programs, including transfer of European marketing rights to a new partner, the terms of such arrangements and contracts, the market launch of ATryn® in the U.S. for HD, the progress of initial clinical trials of ATryn® for AD indications, the results of research and development and preclinical testing of our other proprietary product candidates, and advances in competing products and technologies, as well as general market conditions.

We use our cash primarily to pay salaries, wages and benefits, facility and facility-related costs of office, farm and laboratory space and other outside direct costs such as manufacturing and clinical trial expenses. During 2008 we had a net decrease in cash and marketable securities of $4.1 million, which reflects $18 million used in operations, net of LFB funding of $5.6 million and $550,000 used for capital expenditures, net of $5.4 million received in proceeds from a registered direct offering and $10.4 million in proceeds from the LFB convertible debt transaction. We are currently in discussions for potential new partnering arrangements with a plan to bring in further financial resources. In addition, we may sell additional equity or debt securities. However, there can

be no assurance that we will be able to enter into anticipated partnering arrangements, or raise additional capital, on terms that are acceptable to us, or at all. We estimate that the net use of cash in operations for 2009 to be between $18 million and $22 million. We project receipts of $13 million to $17 million from new or expanded partnership relationships.

At December 28, 2008, we had cash, cash equivalents and marketable securities of $11.6 million compared to $15.8 million at December 30, 2007, and we had negative working capital of $2.3 million at December 28, 2008, compared to negative working capital of $1.7 million at December 30, 2007.

Our consolidated financial statements have been presented on the basis that we are a going concern, which contemplates the continuity of business, realization of assets and the satisfaction of liabilities in the ordinary course of business. We have incurred losses from operations and negative operating cash flow in 2008 and since inception, and we have an accumulated deficit of approximately $304.1 million at December 28, 2008. The primary sources of additional capital raised in 2008, 2007 and 2006 have been equity financings and debt financings. Based on our cash balance as of December 28, 2008, as well as potential cash receipts from existing programs, we believe our resources will be sufficient to fund operations into the second quarter of 2009, including debt service requirements. We expect that future sources of funding may include new or expanded collaboration arrangements and sales of equity or debt securities. If no funds are available, we would have to sell or liquidate the business. If adequate funds are not available, we may be required to delay, reduce the scope of or eliminate our research and development programs, reduce our planned commercialization efforts, or obtain funds through arrangements with collaborators or others that may require us to relinquish rights to certain product candidates that we might otherwise seek to develop or commercialize independently. Additionally, any future equity funding may dilute ownership of our existing equity investors.

Cash Flows from Financing Activities

Equity Financing Activities

In January 2007, we sold LFB 3.6 million shares of our Common Stock at a purchase price of $1.23 (the market closing price on the date of the agreement) per share in connection with the third tranche under the purchase agreement with LFB. We received approximately $4.5 million in proceeds from the sale.

In February 2008, we received approximately $5.4 million in proceeds from a registered direct offering, net of approximately $500,000 in offering costs and fees. In the offering, we sold 6.9 million shares of our common stock at $0.87 per share (rounded price on the date of closing) and 7-year warrants to purchase an aggregate of 6.9 million shares of our common stock at an exercise price of $0.87 per share.

Debt Financing Activities

In December 2008, we completed a $15 million convertible debt financing with LFB pursuant to the terms of a purchase agreement that was signed in October of 2008. Under this agreement, the convertible debt will mature on June 30, 2012, and will bear interest at an annual rate of 8%. The debt may be converted into our common stock at a conversion price of $0.31 per share (the market price of our common stock on the date of signing) at LFB's discretion at any time after June 1, 2009. We have the right to redeem the convertible debt on or before June 1, 2009. We also issued to LFB a 5-year warrant to purchase approximately 23,193,548 shares of our common stock at an exercise price of $0.31 per share. Per the terms of the agreement, if the debt is repaid in full, prior to June 1, 2009, which is at our sole discretion, LFB will have the right to require us to redeem the warrants for an aggregate price of $1.5 million in cash. If the debt is repaid in full upon maturity, we have the option to pay the $1.5 million in shares of our common stock. As a condition of the financing, $4 million of the proceeds were placed in a restricted cash account to secure our existing debt to GE Capital. As of December 28, 2008, LFB held, on an as converted basis, approximately 52.6% of our common stock. Collateral for the loan includes a second priority lien on all of our existing and future acquired assets and a first priority lien on our intellectual property.

In December 2006, we refinanced our term loan with GE Capital in the amount of $10 million, of which $7.1 million was used to pay off an existing loan with GE Capital. There are two separate amortization schedules, the first in the amount of $8 million carries a fixed 10.8% annual interest rate and monthly payments of principal

and interest of approximately $109,000 through December 2011 with a balloon payment of approximately $5.2 million in January 2012. The second in the amount of $2 million carries a fixed 10.84% annual interest rate and monthly payments of principal and interest of approximately $65,000 through January 2010. Collateral for the loan includes a first lien on all of our existing and future acquired assets, excluding intellectual property. Following our further amendment to this loan as part of our December 2008 debt financing with LFB, GE Capital has a second priority lien on our intellectual property.

In December 2006, as part of the second investment tranche related to the LFB agreement, we received $2.6 million in exchange for a five-year convertible note issued to LFB. The note accrues interest at a rate of 2% per annum and automatically converts into shares of our common stock in conjunction with any future common stock offerings at the per share offering price of the respective offering, but only to the extent that any conversion does not result in LFB's holdings exceeding 19.9% of our common stock on an as converted basis. In connection with the closing of our February 2008 registered direct offering, $1.7 million of the principal amount of this note and approximately $40,000 of accrued interest on that principal amount were converted into 2 million shares of our common stock at the rate of $0.87 per share. Based on our effective borrowing rate of 10.8%, we recorded a debt discount of approximately $1.1 million for the difference between the stated interest rate and the effective borrowing rate. The debt discount is being amortized over the five-year term of the note, resulting in additional interest expense of approximately $92,000, $225,000 and $10,000 during fiscal years 2008, 2007 and 2006, respectively.

Cash Flows used in Operating Activities

Cash flows used in operating activities were $18 million and $29.9 million for fiscal 2008 and 2007, respectively. The decrease of $11.9 million is primarily a result of $5.6 million in funding received from LFB which was recorded as a credit to research and development expense in 2008 as compared to $1.2 million in funding received from LFB in 2007 which was recorded as a credit to research and development expense and milestone payments of approximately $5 million received from OVATION which were recorded as deferred revenue during 2008.

Cash Flows from Investing Activities

Cash flows provided by investing activities include $6.6 million in net redemptions of marketable securities in our portfolio, all of which was used to fund operations; $550,000 was used for purchases of capital equipment. We anticipate a slightly higher level of capital expenditures company-wide in 2009 as compared to 2008. We plan to utilize new operating lease lines, if they become available, for a portion of our capital expenditures during 2009. However, we have the ability to delay capital purchases if leasing is unavailable.

Contractual Obligations

The following summarizes our contractual obligations at December 28, 2008, and the effect such obligations are expected to have on our liquidity and cash flow in future periods.

	Less than 1 Year	1 to 3 Years	3 to 5 Years	More than 5 Years	Total
Contractual Obligations:					
Long-term debt obligations, including current portion [1]	$ 1,383	$ 2,087	$ 17,182	$ —	$ 20,652
Operating lease obligations	1,756	1,664	44	—	3,464
Service and sublease agreement with Genzyme	660	—	—	—	660
Total contractual cash obligations	$ 3,799	$ 3,751	$ 17,226	$ —	$ 24,776

(1) Our $20.7 million of outstanding long-term debt at December 28, 2008 includes $8 million owed to GE Capital and $12.7 million in convertible notes owed to LFB net of approximately $700,000 of unamortized debt discounts. Of the $20.7 million, approximately $1.4 million was classified as current. The current portion reflects the amount due through December 2009 on our GE Capital term loan.

We are party to license agreements for certain technologies (see Note 7 to the Notes to Consolidated Financial Statements included in Item 8 of this Annual Report). In July 2001, we reacquired Genzyme's ownership interest in the ATIII LLC joint venture in exchange for a royalty to Genzyme based on our sales of ATryn®, if any, commencing three years after the first commercial sale, up to a cumulative maximum of $30 million. Certain of these other agreements contain provisions for future royalties to be paid on commercial sales of products developed from the licensed technologies. Currently, the amounts payable under these other agreements and any resulting commitments on our behalf are unknown and are not able to be estimated because the level of future sales, if any, is uncertain. Accordingly, they are not included in the preceding table.

New Accounting Pronouncements

In December 2007, the FASB issued SFAS No. 141 (revised 2007), "Business Combinations" ("SFAS 141R"). SFAS 141R establishes principles and requirements for how an acquirer recognizes and measures in its financial statements the identifiable assets acquired, the liabilities assumed, any noncontrolling interest in the acquired entity and the goodwill acquired. SFAS 141R also establishes disclosure requirements to enable the evaluation of the nature and financial effects of the business combination. SFAS 141R is effective as of the beginning of an entity's fiscal year that begins after December 15, 2008, and will be adopted by the Company in the first quarter of fiscal 2009. We anticipate that SFAS 141R will have an impact on our accounting for any future business combinations once adopted, but the effect is dependent upon future acquisitions.

In December 2007, the FASB issued SFAS No. 160, "Noncontrolling Interests in Consolidated Financial Statements—an amendment of ARB No. 51" ("SFAS 160"). SFAS 160 establishes accounting and reporting standards for ownership interests in subsidiaries held by parties other than the parent, the amount of consolidated net income attributable to the parent and to the noncontrolling interest, changes in a parent's ownership interest and the valuation of retained noncontrolling equity investments when a subsidiary is deconsolidated. SFAS 160 also establishes disclosure requirements that clearly identify and distinguish between the interests of the parent and the interests of the noncontrolling owners. SFAS 160 is effective as of the beginning of an entity's fiscal year that begins after December 15, 2008, and will be adopted by the Company in the first quarter of fiscal 2009. We do not anticipate that the adoption of SFAS 160 will have an impact on our financial position and results of operations.

In December 2007, EITF 07-01, Accounting for Collaborative Arrangements Related to the Development and Commercialization of Intellectual Property, or EITF 07-01, was issued. EITF 07-01 prescribes the accounting for collaborations. It requires certain transactions between collaborators to be recorded in the income statement on either a gross or net basis when certain characteristics exist in the collaboration relationship. EITF 07-01 is effective for all of our collaborations existing after January 1, 2009. We do not anticipate that the adoption of EITF 07-01 will have an impact on our accounting for any existing or future collaborative arrangements related to the development and commercialization of intellectual property once adopted.

In April 2008, the FASB issued FSP 142-3, "Determination of the Useful Life of Intangible Assets ("FSP 142-3"). FSP 142-3 amends the factors that should be considered in developing renewal or extension assumptions used to determine the useful life of a recognized intangible asset under FAS 142, "Goodwill and Other Intangible Assets." This change is intended to improve the consistency between the useful life of a recognized intangible asset under FAS 142 and the period of expected cash flows used to measure the fair value of the asset under FAS 141R and other generally accepted accounting principles. The requirement for determining useful lives must be applied prospectively to intangible assets acquired after the effective date, and the disclosure requirements must be applied prospectively to all intangible assets recognized as of, and subsequent to, the effective date. FSP 142-3 is effective for fiscal years beginning after December 15, 2008. We expect that the adoption of FSP 142-3 will have an impact on our accounting for any intangible assets which we may acquire in the future, but the effects are dependent upon future intangible assets.

In May 2008, the FASB issued Staff Position No. APB 14-1, "Accounting for Convertible Debt Instruments That May Be Settled in Cash upon Conversion (Including Partial Cash Settlement)" ("FSP APB 14-1"). FSP APB 14-1 clarifies that convertible debt instruments that may be settled in cash upon conversion (including partial cash

settlement) are not addressed by paragraph 12 of APB Opinion No. 14, "Accounting for Convertible Debt and Debt Issued with Stock Purchase Warrants." Additionally, FSP APB 14-1 specifies that issuers of such instruments should separately account for the liability and equity components in a manner that will reflect the entity's nonconvertible debt borrowing rate when interest cost is recognized in subsequent periods. FSP APB 14-1 is effective for financial statements issued for fiscal years beginning after December 15, 2008, and interim periods within those fiscal years. Early adoption is not permitted. We expect FSP APB 14-1 will have an impact on our accounting for any future convertible debt instruments once adopted, but the effect is dependent upon future convertible debt instruments.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

We have certain fixed rate financial instruments at December 28, 2008, including a term loan, two convertible promissory notes payable and three stand-by letters of credit, all of which are not sensitive to changes in interest rates. Our term loan has a carrying value of $8 million, which approximates its fair value. Two of our stand-by letters of credit totaling $449,360 are required under a facility lease and one letter of credit of $150,000 is in connection with the LEO collaboration. The total of our stand-by letters of credit is recorded as restricted cash. At December 28, 2008, nothing has been drawn down on the stand-by letters of credit. Our convertible note issued to LFB in 2008 had a principal balance of approximately $15 million at December 28, 2008. The proceeds were allocated to the convertible note and a warrant based on their relative fair values resulting in $2.4 million allocated to the warrant and recorded to additional paid in capital. Our five-year convertible note payable to LFB had a principal balance of approximately $800,000 at December 28, 2008. These instruments are not leveraged and are held for purposes other than trading.

For the term loan and the remaining LFB convertible promissory notes outstanding, the table below presents the principal cash payments that exist by maturity date as of December 28, 2008.

	($ in 000's)						
	2009	2010	2011	2012	2013	Thereafter	Total
Term Loan	$ 1,311	$ 708	$ 717	$ 5,113	$ —	$ —	$ 7,849
LFB Convertible Note Payable [1]	—	—	843	—	—	—	843
LFB Convertible Note Payable [2]			12,565				12,565
Total	$ 1,311	$ 708	$ 14,125	$ 5,113	$ —	$ —	$ 21,257

The interest rate on the term loan varies between 10.8% and 10.84% at December 28, 2008 and the interest rates on the LFB convertible notes payable were 2% and 8%, respectively, at December 28, 2008.

(1) Based on our effective borrowing rate of 10.8%, we recorded a debt discount of approximately $1.1 million for the difference between the stated interest rate and the effective borrowing rate. The debt discount is being amortized over the five-year term of the note. The debt discount balance as of December 28, 2008 was approximately $200,000.

(2) We recorded a debt discount of approximately $500,000 for the expenses incurred by us on LFB's behalf. The debt discount is being amortized over the term of the note.

Interest Rate Risk

We do not engage in trading market risk sensitive instruments or purchasing hedging instruments or "other than trading" instruments that are likely to expose us to market risk, whether interest rate, foreign currency exchange, commodity price or equity price risk. We have not purchased options or entered into swaps, or forward or future contracts. Our primary market risk is interest rate risk on our investment portfolio. We estimate that the hypothetical loss in earnings for one year of investments held at December 28, 2008, resulting from a hypothetical 10% increase in interest rates, would not have materially affected net loss or materially affected the fair value of rate sensitive instruments. The hypothetical loss was based on financial instruments we held at December 28, 2008 with variable and fixed interest rates.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

Financial Statements

Response to this item is submitted as a separate section of this Annual Report immediately following Item 15.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Conclusion Regarding the Effectiveness of Disclosure Controls and Procedures

Under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, we conducted an evaluation of our disclosure controls and procedures, as such term is defined under Rule 13a-15(e) promulgated under the Securities Exchange Act of 1934, as amended. Based on this evaluation, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures were effective as of the end of the period covered by this Annual Report.

Changes in Internal Controls

There were no changes in our internal control over financial reporting that occurred during the our most recent fiscal quarter that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rule 13a-15(f). Under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on the framework in *Internal Control – Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on our evaluation under the framework in *Internal Control – Integrated Framework*, our management concluded that our internal control over financial reporting was effective as of December 28, 2008. The effectiveness of our internal control over financial reporting as of December 28, 2008, has been audited by PricewaterhouseCoopers LLP, an independent accounting firm, as stated in their report which is included in the index to this Annual Report under Item 15(a)(1).

ITEM 9B. OTHER INFORMATION

None.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS OF THE REGISTRANT AND CORPORATE GOVERNANCE

The names, ages, titles and biographies of our executive officers are provided under "Executive Officers" in Part I, Item 1 of this Annual Report, and are incorporated herein by reference. Additional information regarding our directors and executive officers is set forth in our Proxy Statement for the Annual Meeting of Stockholders, which is scheduled to be held on May 22, 2009 (the "2009 Proxy Statement") under "Election of Directors" and "Section 16(a) Beneficial Ownership Reporting and Compliance." We have adopted a Code of Business Conduct and Ethics that applies to all of our directors, officers and employees, including

our chief executive officer, chief financial officer, and controllers. The Code is available on our website at http://www.gtc-bio.com/investorinfo/corporategovernance.html. A copy of the Code is also available without charge upon request from the Chief Financial Officer at GTC Biotherapeutics, Inc., 175 Crossing Boulevard, Framingham, MA 01702. If we make any substantive amendments to the Code or grant any waiver from a provision of it, we will disclose the nature of such amendment or waiver on our website at www.gtc-bio.com or in a Current Report on Form 8-K.

ITEM 11. EXECUTIVE COMPENSATION

Information regarding executive compensation is set forth under the Sections entitled "Executive Officer and Director Compensation and Board of Directors Committees" in our 2009 Proxy Statement and is incorporated herein by reference.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

Information regarding security ownership of certain beneficial owners, directors and executive officers is set forth under the Section entitled "Security Ownership of Certain Beneficial Owners and Management" in our 2009 Proxy Statement and is incorporated herein by reference.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, DIRECTOR INDEPENDENCE

Information regarding certain relationships and related transactions is set forth under the Section entitled "Transactions with Related Persons" in our 2009 Proxy Statement and is incorporated herein by reference. See also Note 11 to the Consolidated Financial Statements included in Item 8 of this Annual Report.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

Information regarding auditor fees and services is set forth under the Section entitled "Independent Registered Public Accounting Firm" in our 2009 Proxy Statement and is incorporated herein by reference.

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PART IV

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES

(a) The following documents are filed as part of this Annual Report:

(1) Financial Statements

(2) Financial Statement Schedules

All schedules have been omitted because the required information is not applicable or not present in amounts sufficient to require submission of the schedule, or because the information required is in the consolidated financial statements or the notes thereto.

(3) Exhibits We hereby file and incorporate by reference the exhibits listed in the Exhibit Index immediately following the signature page of this Annual Report.

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders
of GTC Biotherapeutics, Inc.:

In our opinion, the consolidated financial statements listed in the index appearing under Item 15(a)(1) present fairly, in all material respects, the financial position of GTC Biotherapeutics, Inc. and its subsidiaries at December 28, 2008 and December 30, 2007, and the results of their operations and their cash flows for each of the three years in the period ended December 28, 2008 in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 28, 2008, based on criteria established in Internal Control - Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). The Company's management is responsible for these financial statements, for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in Management's Report on Internal Control Over Financial Reporting appearing under Item 9A. Our responsibility is to express opinions on these financial statements and on the Company's internal control over financial reporting based on our integrated audits. We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the financial statements are free of material misstatement and whether effective internal control over financial reporting was maintained in all material respects. Our audits of the financial statements included examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has suffered recurring losses from operations and has limited available funds as of December 28, 2008, which raises substantial doubt about its ability to continue as a going concern. Management's plans in regard to this matter are also described in Note 1. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ PricewaterhouseCoopers LLP
Boston, Massachusetts
February 27, 2009

GTC BIOTHERAPEUTICS, INC.
CONSOLIDATED BALANCE SHEETS
(Dollars in thousands except share amounts)

	December 28, 2008	December 30, 2007
Current assets:		
Cash and cash equivalents	$ 11,643	$ 9,075
Marketable securities	—	6,690
Accounts receivable and unbilled contract revenue	287	240
Inventory	863	—
Other current assets	962	974
Total current assets	13,755	16,979
Property, plant and equipment, net	13,396	14,449
Intangible assets, net	6,249	7,151
Other assets	2,404	1,684
Restricted cash	4,599	450
Total assets	$ 40,403	$ 40,713
Current liabilities:		
Accounts payable	$ 8,024	$ 9,904
Accrued liabilities	5,962	4,571
Short-term deferred contract revenue	688	3,067
Current portion of long-term debt	1,383	1,177
Total current liabilities	16,057	18,719
Long-term deferred contract revenue	9,180	4,433
Long-term debt, net of current portion	6,577	7,850
Long-term convertible note to LFB, net of debt discount	12,692	1,667
Other long-term liabilities	20	20
Total liabilities	44,526	32,689
Commitments and contingencies (see Notes 6 and 8)		
Shareholders' equity (deficit):		
Preferred stock, $.01 par value; 5,000,000 shares authorized: 15,000 shares designated as Series D convertible preferred stock, $.01 par value; 115 and 14,615 shares were issued and outstanding at December 28, 2008 and December 30, 2007	—	—
Common stock, $.01 par value; 210,000,000 shares authorized; 102,964,778 shares and 78,269,186 shares issued and outstanding at December 28, 2008 and December 30, 2007, respectively	1,029	783
Additional paid-in capital	298,963	288,688
Accumulated deficit	(304,115)	(281,450)
Accumulated other comprehensive income	—	3
Total shareholders' equity (deficit)	(4,123)	8,024
Total liabilities and shareholders' equity (deficit)	$ 40,403	$ 40,713

The accompanying notes are an integral part of the consolidated financial statements.

GTC BIOTHERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(Dollars in thousands except share and per share amounts)

	For the Fiscal Years Ended		
	December 28, 2008	December 30, 2007	December 31, 2006
Revenues:			
Service revenue	$ 12,189	$ 9,490	$ 4,159
Product revenue	4,467	4,406	1,969
Total revenue	16,656	13,896	6,128
Costs of revenue and operating expenses:			
Cost of service revenue	4,453	7,163	5,210
Cost of product revenue	4,171	4,398	1,441
Research and development, net of related party reimbursements	21,031	28,925	25,401
Selling, general and administrative	10,208	9,834	9,723
Total cost of revenue and operating expenses	39,863	50,320	41,775
Operating loss	(23,207)	(36,424)	(35,647)
Other income (expense):			
Interest income	184	1,443	1,237
Interest expense	(1,183)	(1,329)	(1,001)
Other income (expense)	1,541	(11)	66
Net loss	$ (22,665)	$ (36,321)	$ (35,345)
Net loss per common share (basic and diluted)	$ (0.23)	$ (0.47)	$ (0.53)
Weighted average number of common shares outstanding (basic and diluted)	98,199,961	77,863,008	66,860,345
Comprehensive loss:			
Net loss	$ (22,665)	$ (36,321)	$ (35,345)
Other comprehensive gain (loss):			
Unrealized holding gain (loss) on available for sale securities	(3)	(3)	49
Comprehensive loss	$ (22,668)	$ (36,324)	$ (35,296)

The accompanying notes are an integral part of the consolidated financial statements.

GTC BIOTHERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF SHAREHOLDERS' EQUITY
(In thousands)

	Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total Shareholders' Equity
	Shares	Amount	Shares	Amount	Amount			
Balance, January 1, 2006	—	$ —	60,648	$ 606	$ 245,930	$ (209,784)	$ (43)	$ 36,709
Net loss						(35,345)		(35,345)
Common stock sold under Employee Stock Purchase Plan			133	2	118			120
Common stock issuance to the GTC Savings and Retirement Plan			165	2	182			184
Common stock issued under GTC Bonus Plan			543	5	554			559
Common stock issued under GTC Director Compensation Plan			6		7			7
Proceeds from the exercise of stock options			5		5			5
Proceeds from the issuance of preferred stock, net of offering costs of $270	15				18,832			18,832
Proceeds from the issuance of common stock, net of offering costs of $1,410			12,000	120	16,005			16,125
Stock grant to employees			120	1	146			147
Stock based compensation					564			564
Unrealized gain on investment							49	49
Balance, December 31, 2006	15	$ —	73,620	$ 736	$ 282,343	$ (245,129)	$ 6	$ 37,956
Net loss						(36,321)		(36,321)
Common stock sold under Employee Stock Purchase Plan			176	2	166			168
Common stock issuance to the GTC Savings and Retirement Plan			279	4	307			311
Common stock issued under GTC Director Compensation Plan			52		55			55
Proceeds from the exercise of stock options			5		4			4
Proceeds from the issuance of common stock			3,630	36	4,446			4,482
Stock based compensation					847			847
Unrealized (loss) on investment							(3)	(3)
Common stock issued for Technology License			278	3	297			300
Common stock issued for legal settlement			225	2	223			225
Balance, December 30, 2007	15	$ —	78,265	$ 783	$ 288,688	$ (281,450)	$ 3	$ 8,024
Net loss						(22,665)		(22,665)
Common stock sold under Employee Stock Purchase Plan			86	2	39			41
Common stock issuance to the GTC Savings and Retirement Plan			421	4	206			210
Common stock issued under GTC Director Compensation Plan			141		52			52
Common stock issued under GTC Bonus Plan			632	6	392			398
Proceeds from the issuance of common stock			6,897	69	5,376			5,445
Stock based compensation					660			660
Unrealized (loss) on investment							(3)	(3)
Warrants issued for services					91			91
Conversion of LFB debt	(14)		16,518	165	3,459			3,624
Balance, December 28, 2008	1	$ —	102,960	$ 1,029	$ 298,963	$ (304,115)	$ —	$ (4,123)

The accompanying notes are an integral part of the consolidated financial statements.

GTC BIOTHERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(Dollars in thousands)

	For the Fiscal Years Ended		
	December 28, 2008	December 30, 2007	December 31, 2006
Cash flows for operating activities:			
Net loss from operations	$ (22,665)	$ (36,321)	$ (35,345)
Adjustments to reconcile net loss from operations to net cash used in operating activities:			
Depreciation and amortization	2,650	3,320	3,488
Stock based compensation	712	902	718
Amortization of premium (discount) on marketable securities	90	57	(369)
Common stock issuance to GTC savings and retirement plan	210	311	184
Inventory write off	—	3,412	1,343
Write off of intangible assets	—	—	497
Loss (gain) on disposal of fixed assets	—	22	—
Non-cash interest expense	115	225	10
Changes in assets and liabilities:			
Accounts receivable and unbilled contract revenue	(47)	45	(81)
Inventory	(863)	(320)	(3,092)
Other assets and liabilities	(520)	40	96
Accounts payable	(1,880)	537	1,932
Accrued liabilities	1,820	(399)	2,275
Deferred contract revenue	2,368	(1,754)	3,714
Net cash used in operating activities	(18,010)	(29,923)	(24,630)
Cash flows from investing activities:			
Purchase of property, plant and equipment	(550)	(1,567)	(1,101)
Purchase of intangible asset	—	(200)	—
Restricted cash	(150)	—	—
Purchase of marketable securities	—	(16,987)	(33,538)
Redemption of marketable securities	6,600	28,716	25,295
Net cash provided by (used in) investing activities	5,900	9,962	(9,344)
Cash flows from financing activities:			
Proceeds from the LFB financing, net of offering costs	—	4,482	20,265
Proceeds from the issuance of common stock, net of offering costs	5,445	—	16,125
Net proceeds from employee stock purchase plan	41	168	120
Net proceeds from the exercise of stock options	—	4	5
Proceeds from long-term debt, net of financing costs	10,403	—	9,760
Repayment of long-term debt	(1,211)	(974)	(13,296)
Net cash provided by financing activities	14,678	3,680	32,979
Net increase (decrease) in cash and cash equivalents	2,568	(16,281)	(995)
Cash and cash equivalents at beginning of the period	9,075	25,356	26,351
Cash and cash equivalents at end of the period	$ 11,643	$ 9,075	$ 25,356
Supplemental disclosure of cash flow information:			
Cash paid during the period for interest	$ 930	$ 961	$ 976
Common stock issuance for Technology License	—	300	—
Conversion of LFB debt, net of debt discount	1,135	—	—
Restricted cash	4,000	—	—
Warrants issued to LFB	2,455	—	—
Assets purchased under capital lease	144	—	—
Common stock issuance for legal settlement	—	225	—

The accompanying notes are an integral part of the consolidated financial statements.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

Fiscal years ended December 28, 2008, December 30, 2007 and December 31, 2006 (all tabular $ in thousands, except per share data).

NOTE 1. NATURE OF BUSINESS

We are the leader in the development and production of human therapeutic proteins through transgenic technology that enables animals to produce what is known as a recombinant form of a specified human protein in their milk. Using this technology, we are developing a portfolio of recombinant blood proteins to treat a range of genetic and acquired blood deficiencies, including hemophilia and other blood coagulation disorders. These blood proteins, also known as plasma proteins, are difficult to produce in other manufacturing systems, and some are currently only available by extraction from human blood. We have also initiated the development of a portfolio of monoclonal antibodies, or MAbs, for use as potential follow-on biologics targeted at several large market products. The level and speed of development of our proprietary programs will be dependent upon our financial resources and new partnering arrangements, as well as progress made in the legislative process related to follow-on biologics.

Our first product, ATryn®, is a recombinant form of human antithrombin, a blood protein with anticoagulation and anti-inflammatory properties. In 2006, ATryn® became the first transgenically produced therapeutic protein to be approved anywhere in the world when we obtained the European Commission's approval of the use of ATryn® as a prophylactic treatment for patients with hereditary antithrombin deficiency, or HD, undergoing surgical procedures. On February 6, 2009, we received United States Food and Drug Administration, or FDA, approval for ATryn® for HD patients undergoing surgery or childbirth, making ATryn® the first transgenically derived therapeutic protein approved by the FDA. The FDA has also designated ATryn® an Orphan Drug in this indication. Along with the approval of ATryn®, the FDA's Center for Veterinary Medicine also approved our New Animal Drug Application, the first of its kind to regulate genetically engineered animals. This is now required for a recombinant technology used to develop transgenic animals, such as the goats that produce recombinant antithrombin. We believe that the regulatory approval of ATryn® in Europe and the U.S. achieved an important validation of our production technology, which will assist in obtaining approvals for other compounds and in other countries.

We plan to develop our portfolio of recombinant proteins through strategic collaborations:

- In June 2008, we entered into a collaboration agreement with OVATION Pharmaceuticals, Inc., or OVATION, to develop and market ATryn® in the United States. The collaboration agreement includes the commercialization of ATryn® in HD, and the further development of ATryn® in acquired antithrombin deficiency indications, or AD.
- In September 2006, we entered into a collaboration agreement with LFB Biotechnologies, or LFB, to develop selected recombinant plasma proteins and MAbs. The first program in this collaboration is for the development of a recombinant form of human blood coagulation factor VIIa for the treatment of patients with hemophilia. This collaboration has now become a legal joint venture, and we have added to the joint venture programs to develop a recombinant form of human blood coagulation factor IX, recombinant human alpha-1 antitrypsin, as well as an antibody to the CD20 immune system receptor, the same target as for the MAb marketed as Rituxan®.

We are subject to risks common to companies in the biotechnology industry, including, but not limited to, the uncertainties of clinical trials and regulatory requirements for approval of therapeutic compounds, the need for additional capital, competitive new technologies, dependence on key personnel, protection of proprietary technology, and compliance with the FDA and other United States and foreign government regulations.

Our consolidated financial statements have been presented on the basis that we are a going concern, which contemplates the continuity of business, realization of assets and the satisfaction of liabilities in the ordinary course of business. We have incurred losses from operations and negative operating cash flow in each fiscal year 2008, 2007 and 2006 and have an accumulated deficit of approximately $304.1 million at December 28, 2008.

We also have negative working capital of $2.3 million as of December 28, 2008. Based on our cash balance as of December 28, 2008, as well as potential cash receipts from existing programs, we believe our capital resources will be sufficient to fund operations into the second quarter of 2009. Our recurring losses from operations and our limited available funds raise substantial doubt about our ability to continue as a going concern. Our plans with regard to this matter include seeking additional financing arrangements and seeking collaboration arrangements. If no funds are available, we would have to sell or liquidate the business. The financial statements do not include any adjustments relating to the recoverability and classification of recorded assets or the amount of reclassification of liabilities, or any adjustments that might be necessary should we be unable to continue as a going concern. The primary sources of additional capital raised in 2008, 2007 and 2006 were equity financings and debt financings. Management expects that future sources of funding may include new or expanded partnering arrangements and sales of equity or debt securities. Adequate additional funding may not be available to us on acceptable terms or at all. Our failure to raise capital as and when needed could have a negative impact on our financial condition and our ability to pursue our business strategies. We may be required to delay, reduce the scope of or eliminate our research and development programs, or obtain funds through arrangements with collaborators or others that may require us to relinquish rights to certain product candidates that we might otherwise seek to develop or commercialize independently. Additionally, any future equity funding may dilute ownership of our existing equity investors.

NOTE 2. SIGNIFICANT ACCOUNTING POLICIES

Basis of Consolidation

The consolidated financial statements include our results, the results of our wholly-owned subsidiaries and our Taurus hSA LLC joint venture. We consolidate the Taurus hSA LLC joint venture for financial reporting purposes. All significant inter-company transactions have been eliminated and we operate in one business segment.

On June 30, 2008, we entered into an additional amendment to the Joint Development and Commercialization Agreement with LFB to establish LFB/GTC LLC as a separate legal entity for the joint venture. Our investment in this joint venture is being accounted for at cost based on our ownership percentage and is not being consolidated in accordance with FASB Interpretation No. 46, Consolidation of Variable Interest Entities, or FIN 46(R), as we are not the primary beneficiary of the joint venture.

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires management to make certain estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. The significant estimates and assumptions in these financial statements include revenue recognition, collectibility of accounts receivable and unbilled revenues, estimates of accrued expenses, valuation of inventory and tax valuation reserves. Actual results could differ materially from those estimates.

Cash and Cash Equivalents

Cash equivalents consist principally of money market funds and municipal notes purchased with initial maturities of three months or less.

Marketable Securities

Marketable securities have been classified as available for sale and are stated at market value based on quoted market prices. Gains and losses on sales of securities are calculated using the specific identification method. Marketable securities can be summarized as follows:

	December 30, 2007	
	Amortized Cost	Estimated Fair Value
Corporate obligations	$ 6,688	$ 6,690
Total marketable securities	$ 6,688	$ 6,690

Maturities of our marketable securities at December 30, 2007 were less than one year.

At December 28, 2008, December 30, 2007 and December 31, 2006 the change in unrealized gain (loss) on marketable securities included in other accumulated comprehensive income and equity was $(3,000), $(3,000) and $49,000, respectively. Realized gains (losses) on available for sale securities in 2008, 2007 and 2006, were immaterial. All of our marketable securities were classified as short-term, which was consistent with their intended use and maturity dates. There were no unrealized losses on marketable securities at December 28, 2008 and December 30, 2007.

Concentration of Credit Risk

Financial instruments that potentially subject us to concentrations of credit risk consist primarily of cash, cash equivalents, marketable securities and trade accounts receivable. At December 28, 2008 and December 30, 2007, approximately 100% of cash, cash equivalents and marketable securities were held by one United States financial institution and exceed federally insured limits.

We perform ongoing credit evaluations of our customers' financial conditions and maintain reserves for potential credit losses. There were no reserves required for 2008, 2007 or 2006, nor were there any write-offs for fiscal 2008, 2007 and 2006.

At December 28, 2008, three customers accounted for 100% of accounts receivable. At December 30, 2007, there were no accounts receivable and at December 31, 2006, one customer accounted for 100% of accounts receivable.

The following table summarizes our revenues by customer / partner as a percent of revenue in the last three years:

	2008	2007	2006
Merrimack	23%	29%	54%
LEO	27%	32%	32%
PharmAthene	39%	28%	—
Other	11%	11%	14%
	100%	100%	100%

Property, Plant and Equipment

Property, plant and equipment are stated at cost and are depreciated using the straight-line method over estimated useful lives of three to thirty years. Leasehold improvements are amortized using the straight-line method over the life of the improvement or the remaining term of the lease, whichever is shorter. The purchase of the New Zealand goats ("Livestock (NZ)") are capitalized and amortized using the straight-line method over their estimated useful lives of five years.

The following is the summary of property, plant and equipment and related accumulated amortization and depreciation as of December 28, 2008 and December 30, 2007.

	Years of Life	December 28, 2008	December 30, 2007
Land	—	$ 909	$ 909
Buildings	20-30	14,135	14,132
Livestock (NZ)	3-5	2,842	2,842
Leasehold improvements	lease life	2,359	2,341
Laboratory, manufacturing and office equipment	3-10	14,092	13,576
Laboratory, manufacturing and office equipment—capital lease	3-10	1,287	1,143
		35,624	34,943
Less accumulated amortization and depreciation		(22,228)	(20,494)
Net property, plant and equipment		$ 13,396	$ 14,449

Depreciation and amortization expense was $1,744,000, $2,432,000 and $2,500,000, for the fiscal years ended December 28, 2008, December 30, 2007 and December 31, 2006, respectively. Accumulated amortization for equipment under capital lease was $1,173,000, $1,127,000 and $1,118,000 at December 28, 2008, December 30, 2007 and December 31, 2006, respectively.

During 2008, we purchased $144,000 of fixed assets and financed these additions with capital lease obligations.

Long-Lived Assets

Management's policy regarding long-lived assets is to evaluate the recoverability of our assets when the facts and circumstances suggest that these assets may be impaired. This analysis relies on a number of factors, including operating results, business plans, budgets, economic projections and changes in management's strategic direction or market emphasis. The test of such recoverability is a comparison of the asset value to its expected cumulative undiscounted net operating cash flow over the remaining life of the asset. If an impairment exists, it is measured by the excess of the carrying value over the cumulative discounted cash flows. Any write-downs are treated as permanent reductions in the carrying amount of the assets.

Share-Based Compensation

We record share-based compensation expense in accordance with SFAS 123(R) Share-Based Payment (or SFAS 123(R)), which requires companies to measure and recognize compensation expense for all share-based payments at fair value over the employees' service periods or the derived service period for awards with market conditions. Compensation expense is measured at fair value of the award at the grant date, including estimated forfeitures, and is adjusted to reflect actual forfeitures and the outcome of certain conditions.

Revenue Recognition and Contract Accounting

We enter into licensing and development agreements with collaborative partners for the development, production and purification of our internally developed recombinant protein candidates or for a transgenically produced version of the partner's therapeutic recombinant proteins. The terms of the agreements typically include non-refundable license fees, funding of research and development, payments for manufacture of drug product, payments based upon the achievement of certain milestones and royalties on future product sales, if any.

We recognize revenue in accordance with Staff Accounting Bulletin No. 101, "Revenue Recognition in Financial Statements" (SAB No. 101), as amended by Staff Accounting Bulletin No. 104, "Revenue Recognition" (SAB No. 104), and Emerging Issues Task Force Issue No. 00-21, "Revenue Agreements with Multiple Deliverables" (EITF No. 00-21).

Revenues from the sale of products and services are recognized when persuasive evidence of an agreement exists, delivery has occurred or services have been rendered, the fees are fixed or determinable, and collectibility is reasonably assured. Revenues from royalties on third-party sales of licensed technologies are generally recognized in accordance with the contract terms when the royalties can be reliably determined and collectibility is reasonably assured.

We assess multiple element revenue arrangements involving upfront payments, license fees, manufacturing services and milestone payments received for the delivery of rights or services. The following criteria must be met for an element to represent a separate unit of accounting:

a) The delivered items have value to a customer on a standalone basis;

b) There is objective and reliable evidence of the fair value of the undelivered items; and

c) Delivery or performance is probable and within our control for any delivered items that have a right of return.

If these criteria are met, we apply the appropriate revenue recognition model as described above to each separate unit of accounting. If these criteria are not met, elements are combined into a single unit of accounting and revenue is not recognized until we have verifiable objective evidence of the undelivered element. Upfront payments and license fees are recognized ratably over the longer of the contractual term or expected relationship period. Payments for the achievement of substantive milestones are recognized when the milestone is achieved. Payments for milestones which are not the result of the achievement of a substantive milestone, are recognized ratably over the longer of the remaining contractual term or expected relationship period.

Revenue is also recognized in accordance with SAB 101 FAQ 13 (EITF 91-6). Under that model, revenue is recognized using the lesser of non-refundable cash received and milestones met or the result achieved using level-of-efforts accounting. The estimated costs to complete each program are based on the contract terms and detailed program plans, including cost projections, of each program under review. All revenue recognition estimates are made based upon the current facts and circumstances and are reassessed on at least a quarterly basis. There are a number of factors which could cause the need for a revision to these estimates, which in turn may have the effect of increasing or decreasing revenue in the current period as they become known. These factors include unforeseen additional costs, delay in a program, efficiencies or decisions at the partner's discretion.

Deferred revenue arises from payments received in advance of the culmination of the earnings process. Deferred revenue expected to be recognized within the next twelve months is classified as a current liability. Deferred revenue will be recognized as revenue in future periods when the applicable revenue recognition criteria have been met.

Inventory

Inventory consists of:

	At December 28, 2008	At December 30, 2007
Finished goods	$ 863	$ —
Total inventory	$ 863	$ —

We carry inventory at the lower of cost or market using the first-in, first-out method. We expect that all inventory which we capitalize will be sold for clinical trials and commercial use. Currently, because we have only two customers, we only capitalize inventory if orders have been received. If at any time we believe that the sale of inventory is no longer probable, we will charge the inventory to expense. Because our current cost of production exceeds our agreed upon maximum price, we are expensing these excess costs as incurred. Inventories on hand at December 28, 2008 were related to ATryn®, which we capitalized after completion of the clinical trials in anticipation of marketing approval for commercial sale in the U.S. The net book value of our inventory as of December 30, 2007 was zero because our estimated cost to complete current orders from LEO exceeded the

agreed upon maximum transfer price. Once our cost of production falls below the agreed upon maximum price, we will capitalize all those costs. We anticipate our cost of production will be substantially reduced as we move to larger production volumes to support clinical and commercial requirements.

During 2007, we wrote off in-process inventory which was rendered unusable as a result of the fill/finish process at the facility of our U.S. based third party fill/finish contractor. We recorded a charge of approximately $2.9 million to cost of sales in connection with the write-off. None of this material had been released for clinical or commercial use. In 2008, we received $1.5 million from the contractor for settlement of this loss which was recorded to other income in 2008. In addition, in 2007, we wrote off in-process inventory which was determined not to meet specifications during release testing for commercial use. We recorded a charge of $469,000 to cost of sales in connection with this write-off.

We analyze our inventory levels quarterly and will write-down inventory that is expected to expire prior to sale, inventory that has a cost basis in excess of its expected net realizable value and inventory in excess of expected requirements. Expired inventory will be disposed of and the related costs will be written off. If actual market conditions are less favorable than those projected by management, additional inventory write-downs may be required. Also, if we should need to use a portion of the capitalized inventory for clinical trials, we would expense the inventory when it was designated for use in such clinical trial.

Research and Development Costs

All research and development costs are expensed as incurred. During our fiscal years ended December 28, 2008, December 30, 2007 and December 31, 2006, we incurred research and development expenses of $21 million, net of $5.1 million funding from LFB, $28.9 million, net of $1.2 million funding, from LFB and $25.4 million, respectively, related to proprietary programs. Of the total spent on research and development, $15.5 million, $21 million and $20.3 million, was spent on the ATryn® development program in fiscal years 2008, 2007 and 2006, respectively, which included manufacturing costs for our U.S. clinical trial and manufacturing costs of clinical material in excess or the maximum selling price to LEO, as well as process development and validation costs for scale up of the ATryn® manufacturing process. These costs include labor, materials, supplies and overhead, as well as certain subcontracted research projects. Also included are the costs of operating the transgenic production facility such as feed and bedding, veterinary costs and utilities.

Net Loss per Common Share

We apply Statement of Financial Accounting Standards No. 128 ("SFAS 128"), *Earnings Per Share* in calculating earnings per share. Potential common shares consist of warrants (see Note 9), stock options (see Note 10) and stock to be issued under the defined contribution retirement plan (see Note 10). We recorded a net loss from operations in 2008, 2007 and 2006, and, therefore, 52.4 million, 35.4 million and 35.6 million of potential common shares, respectively, were not used to compute diluted loss per share, as the effect was antidilutive. We also have two convertible notes payable to LFB Biotechnologies. The first convertible note has a current principal balance of $600,000, net of unamortized debt discount of $200,000, which automatically converts into shares of our common stock in conjunction with any future common stock offerings at the per share offering price of the respective offering. The second convertible note has a current principal balance of $12.1 million, net of unamortized debt discount of $500,000, which may be converted into our common stock at $0.31 per share at LFB's discretion at any time after June 1, 2009. We have the right to redeem the second convertible note on or before June 1, 2009.

Income Taxes

We account for income taxes under the asset and liability method, which requires recognition of deferred tax assets and liabilities for the expected future tax consequences of temporary differences between the financial statement and tax bases of assets and liabilities using the expected enacted tax rates for the year in which the differences are expected to reverse. The measurement of deferred tax assets is reduced by a valuation allowance if, based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

New Accounting Pronouncements

In December 2007, the FASB issued SFAS No. 141 (revised 2007), "Business Combinations" ("SFAS 141R"). SFAS 141R establishes principles and requirements for how an acquirer recognizes and measures in its financial statements the identifiable assets acquired, the liabilities assumed, any noncontrolling interest in the acquired entity and the goodwill acquired. SFAS 141R also establishes disclosure requirements to enable the evaluation of the nature and financial effects of the business combination. SFAS 141R is effective as of the beginning of an entity's fiscal year that begins after December 15, 2008, and will be adopted by the Company in the first quarter of fiscal 2009. We anticipate that SFAS 141R will have an impact on our accounting for any future business combinations once adopted, but the effect is dependent upon future acquisitions.

In December 2007, the FASB issued SFAS No. 160, "Noncontrolling Interests in Consolidated Financial Statements—an amendment of ARB No. 51" ("SFAS 160"). SFAS 160 establishes accounting and reporting standards for ownership interests in subsidiaries held by parties other than the parent, the amount of consolidated net income attributable to the parent and to the noncontrolling interest, changes in a parent's ownership interest and the valuation of retained noncontrolling equity investments when a subsidiary is deconsolidated. SFAS 160 also establishes disclosure requirements that clearly identify and distinguish between the interests of the parent and the interests of the noncontrolling owners. SFAS 160 is effective as of the beginning of an entity's fiscal year that begins after December 15, 2008, and will be adopted by the Company in the first quarter of fiscal 2009. We do not anticipate that the adoption of SFAS 160 will have an impact on our financial position and results of operations.

In December 2007, EITF 07-01, Accounting for Collaborative Arrangements Related to the Development and Commercialization of Intellectual Property, or EITF 07-01, was issued. EITF 07-01 prescribes the accounting for collaborations. It requires certain transactions between collaborators to be recorded in the income statement on either a gross or net basis when certain characteristics exist in the collaboration relationship. EITF 07-01 is effective for all of our collaborations existing after January 1, 2009. We do not anticipate that the adoption of EITF 07-01 will have an impact on our accounting for any existing or future collaborative arrangements related to the development and commercialization of intellectual property once adopted.

In April 2008, the FASB issued FSP 142-3, "Determination of the Useful Life of Intangible Assets ("FSP 142-3"). FSP 142-3 amends the factors that should be considered in developing renewal or extension assumptions used to determine the useful life of a recognized intangible asset under FAS 142, "Goodwill and Other Intangible Assets." This change is intended to improve the consistency between the useful life of a recognized intangible asset under FAS 142 and the period of expected cash flows used to measure the fair value of the asset under FAS 141R and other generally accepted accounting principles. The requirement for determining useful lives must be applied prospectively to intangible assets acquired after the effective date and the disclosure requirements must be applied prospectively to all intangible assets recognized as of, and subsequent to, the effective date. FSP 142-3 is effective for fiscal years beginning after December 15, 2008. We expect that the adoption of FSP 142-3 will have an impact on our accounting for any intangible assets which we may acquire in the future, but the effects are dependent upon future intangible assets.

In May 2008, the FASB issued Staff Position No. APB 14-1, "Accounting for Convertible Debt Instruments That May Be Settled in Cash upon Conversion (Including Partial Cash Settlement)" ("FSP APB 14-1"). FSP APB 14-1 clarifies that convertible debt instruments that may be settled in cash upon conversion (including partial cash settlement) are not addressed by paragraph 12 of APB Opinion No. 14, "Accounting for Convertible Debt and Debt Issued with Stock Purchase Warrants." Additionally, FSP APB 14-1 specifies that issuers of such instruments should separately account for the liability and equity components in a manner that will reflect the entity's nonconvertible debt borrowing rate when interest cost is recognized in subsequent periods. FSP APB 14-1 is effective for financial statements issued for fiscal years beginning after December 15, 2008, and interim periods within those fiscal years. Early adoption is not permitted. We expect FSP APB 14-1 will have an impact on our accounting for any future convertible debt instruments once adopted, but the effect is dependent upon future convertible debt instruments.

NOTE 3. SIGNIFICANT AGREEMENTS

OVATION Pharmaceuticals ("OVATION")

In June 2008, we entered into a collaboration agreement with OVATION Pharmaceuticals, Inc., or OVATION, to develop and market ATryn® in the United States. The collaboration agreement includes the commercialization of ATryn® in the HD indication and the further development of ATryn® in AD. Under the terms of our agreement, OVATION is obligated to make milestone payments to us for a total of $9 million through approval of ATryn® for HD in the U.S., including $5 million paid in 2008 and $4 million expected to be received in the first quarter of 2009. These milestone revenues will be recognized over the life of the agreement on a straight-line basis beginning with the first delivery of ATryn® to OVATION, which is scheduled to occur in the second quarter of 2009. There is a right of return on our first shipment of product to OVATION, therefore we will defer the recognition of revenue until this product shipment has been sold to end users. The collaboration anticipates further development of ATryn® in larger market AD indications, such as the treatment of heparin resistance in patients undergoing surgery requiring cardiopulmonary bypass and the treatment of disseminated intravascular coagulation, or DIC, associated with severe sepsis.

We are responsible for production of ATryn® and will receive a transfer price, including a margin, for commercial product, a royalty on net sales, $257 million in potential clinical, regulatory and sales milestone payments, including $5 million already received, and payment for product used in clinical trials. Our agreement provides for OVATION to further develop ATryn® in AD and to fund our anticipated costs of clinical development. OVATION will be responsible for sales and marketing of ATryn® in the U.S., including all launch activities, which are scheduled to commence in the second quarter of 2009.

LFB Biotechnologies

In September 2006, we entered into a collaboration agreement with LFB, a related party, to develop selected recombinant plasma proteins and MAbs using our transgenic production platform. LFB is a subsidiary of LFB S.A., a vertically integrated plasma fractionation company based in Paris, France that currently markets 19 plasma-derived products in the areas of hemostasis, anesthesia-intensive care and immunology. LFB S.A. is a for-profit company currently 100% owned by the French government. The first program in this collaboration is for the development of rhFVIIa. We have subsequently added to the LFB collaboration programs to develop a recombinant form of human factor IX, an antibody to the CD20 immune system receptor, and recombinant human alpha-1 antitrypsin.

Under this collaboration, we are to share equally with LFB in the cost of the development and commercialization of each product and we will be entitled to 50% of any profits derived from products developed through the joint venture, provided we each contribute equally to the costs of their development. In the event that contributions to development are not equal, the profit allocation will be adjusted based on development costs incurred. Through 2008, LFB has contributed 85% of the costs of the joint venture and owns that same percentage of future profits, subject to our right to reestablish our 50% ownership by repaying LFB our share of the costs plus a specified premium that increases over time as clinical development progresses. During 2008 and 2007, we received approximately $5.6 million and $1.2 million, respectively, in funding from LFB for an agreed portion of our costs incurred in the programs in the joint venture, which was recorded against research and development expenses. Under the agreement, a joint steering committee of each company's representatives determines product development and commercialization plans. We are responsible for development of the production system for the products and retain exclusive commercial rights to the products in North America. LFB is responsible for clinical development and regulatory review of the programs in this joint venture, and has exclusive commercial rights in Europe. We hold co-exclusive rights with LFB in the rest of the world to any products developed through the joint venture. The initial term of the agreement is fifteen years, subject to extension or termination by mutual consent, and the terms for any product developed through the collaboration will continue until the later of the initial term or ten years beyond regulatory approval of that product.

We have amended our agreement with LFB to establish LFB/GTC LLC, as a separate legal entity for the joint venture. This amendment added LFB/GTC LLC as a party to the agreement and provided that rights to the intellectual property of the new joint venture will flow through this entity. All other terms and conditions remain the same. Both parties are performing work under the joint venture and are cross charging their respective expenses incurred to the joint venture. Our investment in the joint venture is being accounted for at cost based on our ownership percentage and is not being consolidated in accordance with FASB Interpretation No. 46, Consolidation of Variable Interest Entities, or FIN 46(R), as we are not the primary beneficiary of the joint venture. As of December 28, 2008, we had a $500,000 payable to the joint venture.

In connection with the collaboration agreement, we entered into a purchase agreement with LFB pursuant to which LFB committed to purchase up to an aggregate of $25 million of shares of convertible preferred stock, shares of common stock and a subordinated convertible note. Each share of preferred stock is convertible into 1,000 shares of common stock at the option of the preferred stock holder any time subsequent to the issuance. The purchase price of the shares of stock was $1.23 per common share equivalent, which was the market value of our common stock on the date of the agreement. These securities were issued and sold in three tranches, or installments, the first of which involved LFB's purchase on October 4, 2006 of 5,000 shares of our newly designated Series D preferred stock representing 5 million common share equivalents at an aggregate purchase price of $6.2 million. In the second tranche, LFB purchased an additional 9,615 shares of Series D preferred stock at an as converted per share price of $1.23 and a subordinated convertible note in the principal amount of approximately $2.6 million, for an aggregate purchase price of approximately $14.4 million.

The convertible note has a term of five years, accrues interest at a rate of 2.0% per annum and will automatically convert into shares of our common stock in conjunction with any future common stock offerings at the per share offering price of the respective offering, but only to the extent that any conversion does not result in LFB's holdings to exceed 19.9% of our common stock on an as converted basis. As sole holder of the Series D preferred stock, LFB became entitled to designate a director to serve on our board. In the third tranche, which closed on January 3, 2007, LFB purchased 3,630,000 shares of common stock at a price of $1.23 per share, for an aggregate purchase price of approximately $4.5 million. Completion of the second and third tranches was subject to our receipt of certain shareholder approvals, which were obtained on December 5, 2006. In connection with the closing of our February 2008 registered direct offering, $1.7 million of the principal amount of the note and approximately $40,000 of accrued interest on that note were converted into 2,018,404 shares of our common stock at a rate of $0.87 per share, representing the fair value of our common stock on the date of conversion.

In December 2008, we completed a $15 million convertible debt financing with LFB pursuant to the terms of a purchase agreement that was signed in October of 2008. Under this agreement, the convertible debt will mature on June 30, 2012, and will bear interest at an annual rate of 8%. The debt may be converted into our common stock at a conversion price of $0.31 per share (the market price of our common stock on the date of signing) at LFB's discretion at any time after June 1, 2009. We have the right to redeem the convertible debt on or before June 1, 2009. Under this agreement, upon conversion of the note in full or in part from time to time, LFB will have the right to designate one or more directors to our Board of Directors, in addition to its current board representative, in proportion to its equity ownership, on a fully diluted basis, provided that in any case, LFB will have the right to appoint the maximum number of directors permissible under Nasdaq requirements. As required by Nasdaq, the number of board representatives would decrease ratably, to the extent that LFB's ownership decreases, such that LFB's board representation would not be disproportional to its equity ownership. The LFB designated directors will be appointed across our three classes of directors in as equal proportions as possible. As long as LFB owns at least 21% of our outstanding common stock on an as-converted basis, LFB's board representatives will be nominated for election at our annual meeting of stockholders.

We also issued to LFB a 5-year warrant to purchase approximately 23,193,548 shares of our common stock at an exercise price of $0.31 per share. Per the terms of the agreement, if the debt is repaid in full prior to June 1, 2009, which is at our sole discretion, LFB will have the right to require us to redeem the warrants for an aggregate price of $1.5 million in cash. If the debt is repaid in full upon maturity, we have the option to pay the $1.5 million in shares of our common stock. Under this agreement, LFB has the right to participate in all of our future offerings of common stock or securities exercisable or convertible into common stock to purchase a number of shares in

proportion to its then *pro rata* ownership of our common stock, on an as converted basis. LFB's participation will be on the terms agreed upon by us and other investors in the future offerings, including price and closing date; provided that LFB will have 10 calendar days upon notice of any offering to choose to participate.

After June 1, 2009, LFB will have a right of first refusal and right of first negotiation with respect to any proposed sale by us of common stock or securities exercisable or convertible into common stock. Pursuant to this right, if we intend to undertake an offering, we must notify LFB of the proposed terms of such offering, and LFB has the right to refuse to purchase the securities on the proposed terms and the right to negotiate with us alternative terms to purchase all of the securities to be sold in the proposed offering. As a condition of the financing, $4 million of the proceeds were placed in a restricted cash account to secure our existing debt to GE Capital. As of December 28, 2008, LFB held, on an as converted basis, approximately 52.6% of our common stock. Collateral for the loan includes a second priority lien on all of our existing and future acquired assets and a first priority lien on our intellectual property.

LEO Pharma A/S ("LEO")

In November 2005, we entered into a collaboration agreement with LEO Pharma A/S for the commercialization of ATryn® in HD in Europe, Canada, and the Middle East and for its further development in AD indications. We received $5 million in non-refundable milestone payments upon entering the collaboration agreement and for achieving approval of ATryn® for the HD indication in Europe. These milestone revenues are being recognized over the life of the agreement on a straight-line basis beginning with the first delivery of ATryn® material to LEO, which occurred in the fourth quarter of 2006. As of December 28, 2008, $4.4 million of the total amount received from LEO was accounted for as deferred revenue. LEO selected DIC associated with severe sepsis as the first AD indication in which to conduct additional clinical studies under this collaboration.

LEO initiated a Phase II dose-ranging study in the DIC indication in 2007. In the third quarter of 2008, LEO advised us that, as a result of an internal re-assessment of their strategic priorities, they wished to enter into negotiations to transfer the ATryn® program to us or an alternate partner. Pending any such transfer, further patients are not being enrolled in the study at this time. LEO made it clear to us that their decision was not based on any safety or efficacy issues.

LEO informed us in September 2008 of their internal reprioritization and desire to transfer the ATryn® program to us or a third party. LEO has attempted to terminate its 2005 collaboration agreement with us for alleged cause before completion of the Phase II study in DIC. However, LEO has made it clear to us that their decision was not based on any safety or efficacy issues. We do not believe that LEO has any basis for such termination, and we further believe that LEO is in breach of the agreement. We initiated International Chamber of Commerce (ICC) arbitration proceedings in the fourth quarter of 2008. We have asked the tribunal to determine that LEO is obligated to perform the agreement, including completion of the Phase II study, and is not legally entitled to exercise its contractual remedies on termination for alleged cause, or alternatively that we are entitled to damages with respect to LEO's actions. While we have sought to conclude this matter by reaching agreements with LEO and a new partner for the collaboration to transfer the DIC trial to a new partner, we believe we are taking necessary and appropriate steps to protect our legal rights through the arbitration process. This process is still in the preliminary stages, and we cannot predict its likely outcome or, in the event of an unfavorable outcome, the potential consequences to us, including cost.

PharmAthene, Inc. ("PharmAthene")

In March 2007, we entered into a process and development and clinical supply manufacturing services agreement with PharmAthene for Protexia® as well as an agreement providing PharmAthene an expanded license to our patent rights, which will support the further development, manufacturing, regulatory approval and commercialization process for PharmAthene's Protexia® program. The development of Protexia® is funded by the United States Department of Defense.

NOTE 4. FAIR VALUE

In September 2006, the Financial Accounting Standards Board (FASB) issued Statement of Financial Accounting Standards No. 157 "Fair Value Measurements" (SFAS 157). SFAS 157 introduces a framework for measuring fair value and expands required disclosure about fair value measurements of assets and liabilities. SFAS 157 for financial assets and liabilities is effective for fiscal years beginning after November 15, 2007, and we have adopted the standard for those assets and liabilities as of December 31, 2007. The adoption of this statement did not have a material impact on our financial position or results of operations. In accordance with the provisions of FSP No. FAS 157-2, "Effective Date of FASB Statement No. 157", we have elected to defer until January 1, 2009 implementation of SFAS 157 as it relates to our non-financial assets and non-financial liabilities that are recognized and disclosed at fair value in the financial statements on a nonrecurring basis.

SFAS 157 defines fair value as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. SFAS 157 also establishes a fair value hierarchy which requires an entity to maximize the use of observable inputs and minimize the use of unobservable inputs when measuring fair value. The standard describes three levels of inputs that may be used to measure fair value:

Level 1 - Quoted prices in active markets for identical assets or liabilities.

Level 2 - Observable inputs other than Level 1 prices such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3 - Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

The Company utilizes the market approach to measure fair value for its financial assets and liabilities. The market approach uses prices and other relevant information generated by market transactions involving identical or comparable assets or liabilities.

Assets and liabilities measured at fair value on a recurring basis are summarized below:

	Fair Value Measure as of December 28, 2008 (dollars in thousands)			
Description	**Total**	**Level 1**	**Level 2**	**Level 3**
Money Market Fund	$ 2,947	$ 2,947	$ —	$ —
Total	$ 2,947	$ 2,947	$ —	$ —

NOTE 5. ACCRUED LIABILITIES

Accrued liabilities included the following:

	At December 28, 2008	At December 30, 2007
Accrued payroll and benefits	$ 2,456	$ 1,922
Accrued bonuses	1,254	814
Amounts owed to third party manufacturer	—	1,532
Other	2,252	303
Total accrued expenses	$ 5,962	$ 4,571

NOTE 6. COMMITMENTS AND CONTINGENCIES

We lease equipment and facilities under various operating and capital leases. Rent expense for the fiscal years ended December 28, 2008, December 30, 2007 and December 31, 2006 was approximately $2,656,000, $2,540,000 and $1,868,000, respectively.

At December 28, 2008, our future minimum payments required under these leases were as follows:

	Operating	Capital
2009	$ 2,416	$ 78
2010	1,366	39
2011	298	—
2012	44	—
2013 and thereafter	—	—
	Operating	**Capital**
Total	$ 4,124	$ 117
Less amount representing interest		6
Present value of minimum lease payments		$ 111

In February 2007, we signed a lease amendment to lease an additional 8,188 square feet of office space which expires in September 2010.

We are a party to license agreements for certain technologies (see Note 7). Several of these agreements contain provisions for the future royalties to be paid on commercial sales of products developed from the licensed technologies. Currently the amounts payable under these agreements and any resulting commitments on our behalf are unknown and cannot be practically estimated since the level of future sales, if any, is uncertain.

Under a Sublease Agreement with Genzyme, we committed to make a minimum annual payment of approximately $660,000 in 2009.

On November 13, 2001, two employees of one of our former subsidiaries filed an action against us in the Court of Common Pleas for Philadelphia County in Pennsylvania seeking damages, declaratory relief and certification of a class action relating primarily to their GTC stock options. On February 15, 2007, the parties agreed to settle these claims under terms which provided that our insurer paid $175,000 in cash and we delivered $225,000 of our Common Stock. We accrued this settlement as of December 31, 2006. We issued 225,000 shares of Common Stock in the settlement at $1.00 per share in 2007. The number of shares of Common Stock which were issued was determined based on the per share market value of the Common Stock on the date of issue after the Court concluded a fairness hearing regarding the settlement.

We maintain our herd of cattle for the Taurus hSA LLC at TransOva Genetics in Iowa under an agreement signed in December 2002. As part of the agreement, TransOva agreed to be compensated partially in equity of Taurus only when, and if, Taurus receives outside third party financing. The amount of equity would be valued under the same terms as such outside financing. Any issuance of Taurus equity to TransOva under the agreement is not expected to result in any material expense to us.

NOTE 7. INTANGIBLE ASSETS

In 1990, we established the SMIG JV joint venture with Sumitomo Metal Industries Group to develop proteins transgenically for Asian markets. In September 2000, we acquired full ownership of the SMIG JV from Sumitomo in exchange for shares of our Common Stock valued at approximately $11.2 million. As a result, we hold the marketing rights to transgenic technology in 18 Asian countries, including Japan. The entire purchase price of $11.2 million was allocated to the value of the marketing rights (SMIG marketing rights), the sole assets of SMIG. These costs are being amortized over the estimated 15-year economic useful life of these rights from the date of purchase. These rights relate to our current business as they allow us to sell transgenic proteins in Asia. Without these rights, we would have been severely limited in our ability to pursue key Asian markets, primarily Japan, and would have had a substantial royalty obligation for any revenues derived from Asia and Europe. We are pursuing opportunities in these markets for our transgenic products in development.

In June 2002, we obtained licenses to technology relative to transgenic milk expression, transgenic cattle technology and nuclear transfer technology from Pharming Group N.V., or Pharming. The license provided for a payment of 1.5 million Euro, or approximately $1.5 million, which was paid in July of 2002. These licenses relate to technology, some of which is currently being used in our ongoing activities and, therefore, their associated costs are reported as an intangible asset and are being amortized over a 15-year period, the remaining life of the underlying patents.

In November 2006, the Management Committee of the Taurus Joint Venture, a joint venture between GTC and Fresenius-Kabi to develop human serum albumin in cattle, agreed that neither GTC nor Fresenius-Kabi would fund the recombinant albumin program during the next 12 months. As a result of prioritizing our resources to other development programs, we are minimizing further investment in this program at this time. We determined that this was an event that triggered an impairment review of our Pharming intangible asset. The Pharming technology includes significant general animal development technology as well as bovine technology. It supports our overall animal transgenic platform including basic promoter technology which is a key component to our transgenic technology platform. We concluded that the estimated value of our intangibles was greater than its net book value at December 31, 2006. Judgments used during the analysis included the estimation of the value of revenues to be achieved from our overall business plan for all products produced transgenically.

In April 2007, we obtained a non-exclusive license from Start Licensing, Inc., or Start, for the patents and patent applications developed by the Roslin Institute to apply nuclear transfer to the production of therapeutic proteins in the milk of transgenic animals. Financial terms include an upfront payment of $500,000, of which $200,000 was paid in cash to Start, and a total of 278,370 shares of our common stock, with an aggregate value of approximately $300,000, were issued, divided equally between Start and Exeter. The license agreement remains in place through the last patent to expire, which is expected to occur in 2016 for the currently issued patents. Accordingly, the $500,000 license fee was recorded as an intangible asset in 2007 and is being amortized using the straight-line method over approximately 9 years. There will also be a royalty payable to Start for the commercialization of any products developed with the patented nuclear transfer technology. Our ATryn® product was not developed using this technology.

Intangible assets consist of:

	Amortization Life	December 28, 2008	December 30, 2007
Marketing rights	15 years	$ 11,210	$ 11,210
Accumulated amortization—marketing rights		(6,228)	(5,480)
Net		4,982	5,730
Technology licenses	9 years to 15 years	2,017	2,017
Accumulated amortization—technology licenses		(750)	(596)
Net		1,267	1,421
Total intangible assets, net		$ 6,249	$ 7,151

Amortization expense was $902,000, $888,000 and $988,000 in 2008, 2007 and 2006, respectively.

At December 28, 2008, the estimated aggregate amortization expense was as follows:

2009	$ 902
2010	$ 902
2011	$ 902
2012	$ 902
2013	$ 902
2014 and thereafter	$ 1,739

NOTE 8. BORROWINGS

In December 2006, we entered into a new term loan with GE Capital in the amount of $10 million, of which $7.1 million was used to pay off a previous loan from GE Capital. In connection with the new term loan, we were required to provide $450,000 of cash collateral for two of our outstanding stand-by letters of credit, which appears as restricted cash on the balance sheet. There are two separate amortization schedules. The first, in the amount of $8 million, carries a fixed 10.8% annual interest rate and monthly payments of principal and interest of approximately $109,000 through December 2011 with a balloon payment of approximately $5.2 million in January 2012. The second, in the amount of $2 million, carries a fixed 10.84% annual interest rate and monthly payments of principal and interest of approximately $65,000 through January 2010. Collateral for the loan includes a first lien on all of our existing and future acquired assets and a second lien on our intellectual property.

In December 2006, as part of the second tranche under the LFB agreement, we issued to LFB a $2.6 million, five-year convertible note (see Note 3). Based on our effective borrowing rate of 10.8%, we recorded a debt discount of approximately $1.1 million for the difference between the stated interest rate and the effective borrowing rate. The debt discount is being amortized over the five year term of the note, resulting in additional interest expense of approximately $92,000, $225,000 and $10,000 during fiscal years 2008, 2007 and 2006, respectively.

In December 2008, we completed the sale of a $15 million convertible note and a warrant to LFB (see Note 3). The proceeds of the $15 million were allocated to the convertible note and the warrant based on their relative fair values. Based on a relative fair value allocation, we recorded approximately $2.5 million to additional paid in capital which is being amortized over the term of the note, resulting in additional interest expense of $19,000 during fiscal year 2008. We issued to LFB a 5-year warrant to purchase 23,193,548 shares of our common stock at an exercise price of $0.31 per share. Per the agreement, if the debt is repaid in full, prior to June 1, 2009, which is at our sole discretion, LFB will have the right to require us to redeem the warrant for an aggregate price of $1.5 million in cash. If the debt is repaid in full upon maturity, we have the option to pay the $1.5 million in shares of our common stock. In connection with the agreement, we recorded a debt discount of approximately $500,000 for costs incurred by us on LFB's behalf. The debt discount is being amortized over the term of the note, resulting in additional interest expense of approximately $4,000 during fiscal year 2008. As of December 28, 2008, LFB held, on an as converted basis, approximately 52.6% of our common stock. Collateral for the loan includes a second priority lien on all of our existing and future acquired assets and a first priority lien on our intellectual property.

Our long-term debt consisted of the following:

	December 28, 2008	December 30, 2007
GE Capital loan, with monthly payments of approximately $109 through December 2011, fixed annual interest rate of 10.8%, collateralized by all existing and future acquired assets, excluding intellectual property	$ 7,051	$ 7,571
GE Capital loan, with monthly payments of approximately $65 through January 2010, fixed annual interest rate of 10.84%, collateralized by all existing and future acquired assets, excluding intellectual property	798	1,456
Capital leases, with monthly payments of approximately $6 through July 2010	111	
Convertible note to LFB, fixed annual interest of 2%, net of debt discount [1]	623	1,667
Convertible note to LFB, fixed annual interest of 8%, net of debt discount [2]	12,069	
	20,652	10,694
Less current portion	1,383	1,177
	$ 19,269	$ 9,517

Maturities of long-term debt are as follows:

2009	$ 1,383
2010	747
2011	1,340
2012	17,182
2013 and thereafter	—
	$ 20,652

(1) Based on our effective borrowing rate of 10.8%, we recorded a debt discount of approximately $1.1 million for the difference between the stated interest rate and the effective borrowing rate. The debt discount is being amortized over the five-year term of the note. The debt discount balance as of December 28, 2008 is approximately $200,000.

(2) We recorded a debt discount of approximately $500,000 for the expenses incurred by us on LFB's behalf. The debt discount is being amortized over the term of the note.

At December 28, 2008, the fair values of our debt instruments were as follows:

	(dollars in thousands)
GE Capital loan due December 2011	$ 6,379
GE Capital loan due January 2010	678
Convertible note to LFB, fixed annual interest of 2%	609
Convertible note to LFB, fixed annual interest of 8%	11,685

The fair values of our GE Capital loans and our LFB convertible notes were calculated using a net present value approach using *Level 3* - Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities, under SFAS 157.

NOTE 9. STOCKHOLDERS' EQUITY

Authorized Shares

Our authorized capital stock consists of 210,000,000 shares of Common Stock, par value $0.01 per share, and 5,000,000 shares of preferred stock, par value $0.01 per share, of which 75,000 shares are designated as Series C Junior Participating Convertible Preferred Stock (the Series C Preferred Stock) and 15,000 shares are designated as Series D Preferred Stock, par value $0.01 per share. In March 2001, our Board of Directors restored all unissued or reacquired shares of our Series A Preferred Stock and Series B Preferred Stock to the status of authorized but undesignated and unissued shares of preferred stock.

Shareholder Rights Plan

On May 31, 2001, our Board of Directors adopted a Shareholder Rights Plan (the "Plan") as set forth in the Shareholder Rights Agreement, dated May 31, 2001, between GTC and American Stock Transfer and Trust Company, as Rights Agent (the "Rights Agreement"). A series of our preferred stock, designated as Series C Preferred Stock, par value $0.01 per share, was created in accordance with the Rights Agreement. The Plan is designed to deter coercive takeover tactics, including the accumulation of shares in the open market or through private transactions, and to prevent an acquirer from gaining control of GTC without offering a fair and adequate price and terms to all of our shareholders. As such, the Plan enhances the Board of Directors' ability to protect shareholder interests and ensure that shareholders receive fair and equal treatment in the event any proposed takeover of GTC is made in the future. Pursuant to the Rights Agreement, the Board of Directors declared a dividend distribution of one preferred stock purchase right for each outstanding share of our Common Stock to shareholders of record as of June 1, 2001. The preferred stock purchase rights are attached to, and will trade with, our Common Stock. The purchase rights are currently exercisable upon the occurrence of certain triggering events described in the Rights Agreement. In connection with our transactions with LFB, our Board of Directors amended the Plan to provide that LFB would be excluded from the forfeiture provisions of the Plan so long as it only purchased our securities directly from us.

Common Stock Placements

In July 2006, we sold 12 million shares of our Common Stock to institutional investors in a registered direct offering at $1.38 per share and 10-year warrants to purchase an aggregate of 7,800,000 shares of our Common Stock at an exercise price of $1.4145 per share. The shares and warrants (including the shares issuable upon exercise of the warrants) were issued under a shelf registration statement. We received approximately $16.2 million in proceeds from this sale, net of approximately $1.3 million in offering costs and fees.

In August 2006, our Board of Directors, through the Compensation Committee, approved the issuance of 1,000 shares of common stock to every employee of GTC employed as of June 2, 2006, the date we received the positive opinion from EMEA. As a result, we issued a total of 120,028 shares and recorded compensation expense of approximately $147,000 in the third quarter of 2006.

In January 2007, we sold 3.6 million shares of our Common Stock at a purchase price of $1.23 to LFB in connection with the third tranche under our securities purchase agreement with LFB. We received approximately $4.5 million in proceeds from the sale. In addition, we issued to LFB a $2.6 million, five-year convertible note which is convertible into common stock on terms described in Note 3.

In February 2008, we received approximately $5.4 million in proceeds from a registered direct offering, net of approximately $500,000 in offering costs and fees. In the offering, we sold 6,896,552 million shares of our common stock at $0.87 per share (rounded price on the date of closing) and 7-year warrants to purchase an aggregate of 6,896,552 shares of our common stock at an exercise price of $0.87 per share.

In December 2008, we issued to LFB a $15 million, a convertible note which matures on June 30, 2012 which is convertible into common stock on terms described in Note 3 and a five-year warrant to purchase 23,193,548 shares of our common stock at an exercise price of $0.31 per share.

Preferred Stock Placements

In October 2006, we sold 5,000 shares of our newly designated Series D preferred stock, representing 5 million common share equivalents, to LFB for aggregate proceeds of $6.1 million in connection with the first tranche under the purchase agreement with LFB (see Note 3).

In December 2006, we sold 9,615 shares of Series D preferred stock at a purchase price of $1.23, representing 9.6 million common share equivalents, to LFB for aggregate proceeds of $11.8 million in connection with the second tranche under the purchase agreement with LFB (see Note 3).

Offering costs and fees in conjunction with the two Series D preferred stock placements to LFB were approximately $270,000.

Warrants

A summary of our outstanding warrants for the purchase of common stock as of December 28, 2008, of which 43,653,583 are currently exercisable, is as follows:

Common Shares Issuable for	Exercise Price Per Share	Warrant Expiration Date
55,833	$ 6.30	November 12, 2009
29,491	$ 6.30	November 22, 2009
1,828,573	$ 1.34[1]	February 10, 2011
3,640,762	$ 2.05	December 13, 2010
7,800,000	$ 1.4145	July 18, 2016
6,896,552	$ 0.87	February 7, 2015
58,824	$ 0.71	April 16, 2013
150,000	$ 0.61	May 6, 2013
23,193,548	$ 0.31	December 10, 2013
—		
43,653,583		

(1) The exercise price of these warrants, which was originally $2.52 per share, is subject to anti-dilution adjustments upon the occurrence of certain subsequent equity issuances. Giving effect to the most recent adjustment that occurred as a result of our registered debt financing with LFB in December 2008, the current exercise price of these warrants is $1.34 per share.

At the time of issuance, the warrants were assessed under Emerging Issues Task Force 00-19, "Accounting for Derivative Financial Instruments, Indexed to, and Potentially Settled in, a Company's Own Stock ("EITF 00-19"), and were recorded as a credit to additional paid in capital.

As of December 28, 2008, we have reserved 53,468,134 shares of Common Stock, subject to adjustment, for future issuance under the various classes of warrants, the Equity Plan and Employee Stock Purchase Plans.

NOTE 10. EMPLOYEE BENEFIT PLANS

Equity Plan and Stock Purchase Plan

In May 1993, the Board of Directors adopted and the shareholders approved the 1993 Equity Incentive Plan and the 1993 Director Stock Option Plan (collectively, our "Prior Equity Plan"). In May 2002, our shareholders approved the 2002 Equity Incentive Plan (together with the Prior Equity Plan, the "Equity Plan"), authorizing a total of 2,500,000 shares for issuance to our employees, consultants and directors and to our affiliates. In 2004, 2007 and 2008, our shareholders approved increases of 2,000,000 shares, or 6,000,000 in total, in the number of shares authorized for future issuance under the Equity Plan. In May 2007, our shareholders also approved an automatic annual increase in the number of shares of our common stock available for issuance under the Equity Plan, which annual increase will be added on December 31 of each year beginning in 2008, and will be equal to 1,500,000 shares, or such lesser amount as may be determined by our Board; provided that any increase will not cause the maximum number of shares that may be issued under the Equity Plan to exceed the lesser of 10% of the shares of common stock outstanding as of the date of issuance (including, on an as-converted basis, all outstanding Series D preferred stock convertible into common stock), or 10% cap; and 15,000,000 shares (subject to adjustment in the event of stock splits and other similar events). In December 2008, our shareholders approved an additional 2,000,000 share increase in the Equity Plan and an amendment to the automatic adjustment provision so that the 10% cap includes shares issuable upon conversion of any convertible debt, as long as such convertible debt is convertible without payment of additional consideration by the holder. In addition, 4,340,000 shares subject to options previously granted under our Prior Equity Plans were transferred to our Equity Plan. A total of 8,861,056 shares are subject to outstanding options or reserved for issuance under our Equity Plan, including 8,229,194 options and 608,175 restricted stock units issued under our equity plans outstanding at December 28, 2008. Shares that became available upon termination of forfeited or expired options under our Prior Equity Plan will be added to reserve under our Equity Plan.

In June 2008, we established a Retention Incentive Plan, or Retention Plan, the purpose of which is to encourage the continued employment of our executive officers and other senior personnel through the grant of equity awards and other payments conditioned on continued employment with the Company. Our Compensation Committee is administering the Retention Plan and has the authority to determine the individual participants and the amount of any awards under the Retention Plan. Eligible participants besides our executive officers include Vice Presidents, Senior Directors, Directors and Associate Directors.

Participants in the Retention Plan are eligible to receive awards of restricted stock units issued pursuant to our Equity Plan. We granted 615,825 restricted stock units during 2008. For recipients of those units we also granted 102,600 additional restricted stock units in January 2009. The restricted stock units awarded under the Retention Plan will not become vested and settle until June 30, 2009, provided the participant remains an employee until that date. If we terminate a participant's employment without cause (as provided in the Retention Plan) prior to June 30, 2009, all of the participant's restricted stock units shall become fully vested on the date of the participant's termination of employment.

Participant's in the Retention Plan who remain employed by us through March 31, 2010 will also receive a specified retention payment, payable at the discretion of our Compensation Committee either in a lump sum cash payment or in shares of our common stock. If the payment is made in shares of our common stock, the plan provides for specified minimum valuation levels of our common stock, depending on the employee's level of seniority, which will be used in determining the number of shares to be issued in lieu of cash.

If we terminate a participant's employment without cause prior to March 31, 2010, the participant will be entitled to receive his or her retention payment within 30 days following the date of termination.

In December 2008, we granted 2,225,000 stock options to our executive officers and other senior personnel pursuant to a retention plan under our Equity Plan. The options give the right to purchase our common stock for $0.31 per share. Fifty percent of the options will vest on September 30, 2009 and the remaining options will vest on June 30, 2010.

Under our Equity Plan, shares of Common Stock are reserved for issuance pursuant to incentive stock options, non-statutory stock options, restricted stock awards, stock appreciation rights, restricted stock units or stock units in accordance with specific provisions to be established by a committee of the Board of Directors at the time of grant. The Equity Plan also permits us to assume outstanding options in an acquisition without using shares reserved under the Plan. Annual grants to any individual participant are limited to 400,000 shares for any current participant and 600,000 shares for any new hire, in each case subject to adjustment for changes in our capitalization. No options will have a term that can exceed ten years and awards will be subject to a minimum three-year vesting schedule with exceptions in the discretion of the Compensation Committee for retirement, death, disability, termination by GTC, retention, change in control, grants to consultants, directors or new hires, awards in lieu of cash compensation and performance vesting.

Under our Equity Plan, an option's maximum term is ten years and it vests ratably 20% on the date of issuance and 20% thereafter on the anniversary of the grant.

At December 28, 2008, a total of 23,687 shares were available for grant under our Equity Plan.

A summary of the status of our stock options as of December 28, 2008 and changes during the year then ended is presented below:

	Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term
Outstanding at December 30, 2007	5,910,052	$ 3.56	
Granted	2,970,845	0.38	
Exercised	—		
Cancelled	(651,703)	5.32	
Outstanding at December 28, 2008	8,229,194	$ 2.27	5.45
Options exercisable at December 28, 2008	4,577,173	$ 3.64	4.79
Options vested and those expected to vest at December 28, 2008	7,970,458	$ 2.33	5.42

The aggregate intrinsic value related to the options outstanding, exercisable, exercised and vested is immaterial for 2008, 2007 and 2006.

A summary of the status of our restricted stock units as of December 28, 2008 and changes during the year then ended is presented below:

	Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term
Outstanding at December 30, 2007	—	$ —	
Granted	615,825	—	
Released and issued	—		
Cancelled	(7,650)	—	
Outstanding at December 28, 2008	608,175	$ —	0.51
Restricted stock units exercisable at December 28, 2008	—	$ —	
Restricted stock units vested and those expected to vest at December 28, 2008	608,175	$ —	0.51

The aggregate intrinsic value related to the restricted stock units outstanding, exercisable, exercised and vested is immaterial for 2008.

Included within the statements of operations are the following charges for share-based compensation, which includes both options and restricted stock units:

	(dollars in thousands)		
	December 28, 2008	December 30, 2007	December 31, 2006
Research and development expense	$ 293	$ 359	$ 312
Selling, general and administrative expense	367	488	254
Total share-based compensation	$ 660	$ 847	$ 566

We use the Black-Scholes option-pricing model to estimate fair value of share-based awards with the following weighted average assumptions:

	Fiscal year ended		
	December 28, 2008	December 30, 2007	December 31, 2006
Stock Options and Awards:			
Expected life	6.5 years	6 years	6 years
Expected volatility	87.93%	89.03%	90%
Dividend yield	0%	0%	0%
Risk-free interest rate	1.97%	3.80%	4.63%

In fiscal year ended December 31, 2006, we calculated expected life for stock options and other equity awards using the Staff Accounting Bulletin No. 107, or SAB 107, simplified method. In fiscal year ended December 28, 2008 and December 30, 2007, we calculated expected life for stock options and other equity awards based on the observed and expected time to post-vesting forfeiture and exercise.

We calculate expected volatility for stock options and other equity awards using historical volatility with a look back period over the expected life.

The weighted average estimated fair value at the date of grant for options granted during 2008, 2007 and 2006 was $0.38, $1.09 and $1.04, respectively.

As of December 28, 2008, there was approximately $814,071 of total unrecognized compensation costs related to unvested stock options. This cost is expected to be recognized over a weighted average period of 1.75 years.

As of December 28, 2008, there was approximately $139,226 of total unrecognized compensation costs related to unvested restricted stock units. This cost is expected to be recognized over a weighted average period of 0.51 years.

Shares issued under the Equity Plan, whether for the exercise of stock options or other equity issuances, will be new shares of common stock as authorized under the plan.

In May 2003, our board of directors adopted and our shareholders approved our 2003 Employee Stock Purchase Plan (the "2003 Purchase Plan"). Under the 2003 Purchase Plan, 750,000 shares of Common Stock were reserved for the grant of purchase rights to employees in one or more offerings in accordance with provisions to be established by a committee of the Board of Directors prior to commencement of any offering period. In June 2008, the shareholders approved an increase of 1,000,000 shares under the plan. Participants may purchase shares of Common Stock at not less than 85% of the lower of the market value at the beginning of each offering or on the purchase date. Under the 2003 Purchase Plan, the Compensation Committee has established separate three-month offerings every three months. The stock will be purchased quarterly and each participant can purchase up to 1,260 shares per quarter, subject to an overall limitation of 62,550 shares that may be sold under the 2003 Purchase Plan in any quarter.

We record the FAS 123R compensation expense related to the 2003 Purchase Plan, however, the amounts are immaterial for the fiscal years ended December 28, 2008, December 30, 2007 and December 31, 2006. Therefore, we do not disclose the weighted average assumptions related to the 2003 Purchase Plan.

401(k) Plan

All of our employees, subject to certain eligibility requirements, can participate in our defined contribution plan. Currently, we may match up to 50% of each participating employee's contributions to the plan to a maximum of 3% of salary. We may also contribute an additional 2% of each employee's salary as a retirement contribution. All contributions are at the discretion of the Board of Directors. Expense recognized under this plan was approximately $793,000, $389,000 and $249,000 for the fiscal years ended December 28, 2008, December 30, 2007 and December 31, 2006, respectively.

NOTE 11. INCOME TAXES

A reconciliation of the U.S. federal statutory tax rate to the effective tax rate is as follows:

	Fiscal Years Ended		
	December 28, 2008	December 30, 2007	December 31, 2006
Federal tax—expense (benefit)	(34.0)%	(34.0)%	(34.0)%
State taxes—net	(5.8)	(5.9)	(5.2)
Research and development tax credits	(1.2)	(1.0)	(3.7)
Other	1.3	3.9	1.0
Change in valuation allowance	39.7	37.0	41.9
Effective tax rate	0%	0%	0%

Deferred tax assets and deferred tax liabilities are recognized based on temporary differences between the financial reporting and tax basis of assets and liabilities using future expected enacted rates. A valuation allowance is recorded against deferred tax assets if it is more likely than not that some or all of the deferred tax assets will not be realized.

The components of the deferred tax assets and liabilities at December 28, 2008 and December 30, 2007, respectively, are as follows (dollars in thousands):

	December 28, 2008	December 30, 2007
Deferred tax assets/(liabilities):		
Net operating loss carryforwards	$ 88,784	$ 85,076
Capitalized research and development expenses	20,507	21,967
Tax credits	8,992	8,689
Advance payments	3,974	3,020
Inventory	619	1,810
Accrued compensation	949	301
Other accruals	83	191
Other	185	187

	December 28, 2008	December 30, 2007
Depreciation	(626)	(868)
Total gross deferred tax asset	123,467	120,373
Valuation allowance	(123,467)	(120,373)
Net deferred tax asset	$ —	$ —

As of December 28, 2008, we had federal and state net operating losses ("NOLs") of $239 million and $111 million, respectively, and federal and state research and experimentation credit carryforwards of approximately $6.8 million and $3.3 million, respectively, which will expire at various dates starting in 2008 through 2027. We had approximately $14.1 million of federal net operating losses generated in 1993 and approximately $15.4 million of Massachusetts net operating losses generated in 2002 that expired in 2008. As required by SFAS No. 109, we have evaluated the positive and negative evidence bearing upon the realizability of our deferred tax assets, and we have determined that is more likely than not that we will not recognize the benefits of the deferred tax assets. Accordingly, a valuation allowance of approximately $123 million has been established at December 28, 2008.

Utilization of the NOL and R&D credit carryforwards may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986 due to ownership change limitations that have occurred previously or that could occur in the future. These ownership changes may limit the amount of NOL and R&D credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. We have not currently completed a study to assess whether an ownership change has occurred, or whether there have been multiple ownership changes since our formation, due to the significant complexity and related costs associated with such study. There also could be additional ownership changes in the future which may result in additional limitations in the utilization of the carryforward NOL's and credits.

We have recorded a deferred tax asset of approximately $4.9 million reflecting the benefit of deductions from the exercise of stock options which as been fully reserved until it is more likely than not that the benefit will be realized. The benefit from this $4.9 million deferred tax asset will be recorded as a credit to additional paid-in capital if and when realized through a reduction of cash taxes.

In June 2006, the FASB issued Interpretation No. 48, "Accounting for Uncertainty in Income Taxes, an interpretation of FAS 109" ("FIN 48"). This statement clarifies the criteria that an individual tax position must satisfy for some or all of the benefits of that position to be recognized in a company's financial statements. We adopted FIN No. 48 on January 1, 2007. The implementation of FIN No. 48 did not have a material impact on our consolidated financial statements, results of operation or cash flows. At the adoption date of January 1, 2007, and also at December 28, 2008, we had no unrecognized tax benefits. We have not, as yet, conducted a study of our research and development credit carryforwards. This study may result in an adjustment to our research and development credit carryforwards, however, until such a study is completed and any adjustment is known,

no amounts are being presented as uncertain tax positions under FIN No. 48. A full valuation allowance has been provided against our research and development credits and, if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance. Thus, there would be no impact to the consolidated balance sheet or statement of operations if an adjustment were required.

The tax years 1993 through 2008 remain open to examination by major taxing jurisdictions to which we are subject, which are primarily in the United States, as carryforward attributes generated in years past may still be adjusted upon examination by the Internal Revenue Services or state tax authorities if they have or will be used in a future period. We are currently not under examination by the Internal Revenue Service or any other jurisdiction for any tax years. We would recognize both accrued interest and penalties related to unrecognized benefits in income tax expense. We have not recorded any interest or penalties on any unrecognized tax benefits since inception.

NOTE 12. ARRANGEMENTS WITH RELATED PARTIES

LFB Biotechnologies ("LFB")

In September 2006, we entered into a collaboration agreement with LFB to develop selected recombinant plasma proteins and MAbs using our transgenic production platform. We also entered into a stock and note purchase agreement in September 2006 and a note and warrant purchase agreement in December 2008, which provides for certain ongoing arrangements with LFB (see Note 3).

NOTE 13. GEOGRAPHICAL INFORMATION

Net revenues from external customers are based on the location of the customer.

Geographic information for net revenues from external customers, by fiscal year, is presented in the table below:

	United States	Europe	Israel	Total
2008	$ 12,189	$ 4,467	$ —	$ 16,656
2007	9,485	4,406	5	13,896
2006	4,156	1,969	3	6,128

Of our long-lived assets, $5 million of intangible assets (net) are located in the Cayman Islands.

Geographic information for all other long lived assets, by fiscal year, is presented in the table below:

	United States	United Kingdom	New Zealand	Total
2008	$ 14,488	$ 5,911	$ —	$ 20,399
2007	11,000	5,495	88	16,583

NOTE 14. UNAUDITED RESULTS OF QUARTERLY OPERATIONS

	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
2008				
Revenue	$ 3,545	$ 9,139[1]	$ 2,929	$ 1,043
Operating loss	(8,197)	(1,825)[2]	(5,831)[3]	(7,353)[4]
Net loss	(8,223)	(2,213)	(6,060)	(6,168)[5]
Net loss per share—basic and diluted	(0.10)	(0.02)	(0.06)	(0.06)
	First Quarter	**Second Quarter**	**Third Quarter**	**Fourth Quarter**
2007				
Revenue	$ 5,429[6]	$ 2,838	$ 2,576	$ 3,052
Operating loss	(7,758)	(10,677)[7]	(8,280)	(9,709)[8]
Net loss	(7,509)	(10,592)	(8,388)	(9,832)
Net loss per share—basic and diluted	(0.10)	(0.14)	(0.11)	(0.13)

(1) In the second quarter of 2008, we recognized $4.2 million of revenue from product shipments to LEO.

(2) In the second quarter of 2008, we received $3 million of funding from LFB for costs incurred during the first six months of 2008 which was recorded as a contra expense to research and development.

(3) In the third quarter of 2008, we received $1.2 million of funding from the LFB/GTC LLC for costs incurred during the third quarter of 2008.

(4) In the fourth quarter of 2008, we received $900,000 of funding from the LFB/GTC LLC for costs incurred during the fourth quarter of 2008.

(5) In the fourth quarter of 2008, we received $1.5 million from the settlement of arbitration related to the fill/finish process conducted at a U.S. based third party fill/finish contractor during 2007.

(6) In the first quarter of 2007, we recognized $3.3 million of revenue from product shipments to LEO.

(7) In the second quarter of 2007, we wrote off $2.9 million related to in-process inventory which was rendered unusable as a result of the fill/finish process at the facility of our U.S. based third party fill/finish contractor.

(8) In the fourth quarter of 2007, we began processing additional material for LEO.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized, in Framingham, Massachusetts on the 27th day of February 2009.

GTC BIOTHERAPEUTICS, INC.

By: /s/ Geoffrey F. Cox
Geoffrey F. Cox
Chairman of the Board, President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934 this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the date indicated.

Signature	Title	Date
/s/ Geoffrey F. Cox Geoffrey F. Cox	Chairman of the Board, President and Chief Executive Officer (Principal Executive Officer)	February 27, 2009
/s/ John B. Green John B. Green	Chief Financial and Accounting Officer (Principal Financial and Accounting Officer)	February 27, 2009
/s/ Robert W. Baldridge Robert W. Baldridge	Director	February 27, 2009
/s/ Kenneth A. Bauer Kenneth A. Bauer	Director	February 27, 2009
/s/ Christian Béchon Christian Béchon	Director	February 27, 2009
/s/ Francis J. Bullock Francis J. Bullock	Director	February 27, 2009
/s/ James A. Geraghty James A. Geraghty	Director	February 27, 2009
/s/ Mary Ann Gray Mary Ann Gray	Director	February 27, 2009
/s/ Michael J. Landine Michael J. Landine	Director	February 27, 2009
/s/ Pamela W. McNamara Pamela W. McNamara	Director	February 27, 2009
/s/ Marvin L. Miller Marvin L. Miller	Director	February 27, 2009
/s/ Alan W. Tuck Alan W. Tuck	Director	February 27, 2009

EXHIBIT INDEX
to Form 10-K for the Year Ended December 28, 2008

Exhibit No.	Description
3.1.1	Restated Articles of Organization of GTC filed with the Secretary of the Commonwealth of Massachusetts on December 27, 1993. Filed as Exhibit 3.1 to GTC's Annual Report on Form 10-K for the year ended December 31, 1993 (File No. 0-21794) and incorporated by reference herein.
3.1.2	Articles of Amendment to the Restated Articles of Organization of GTC filed with the Secretary of the Commonwealth of Massachusetts on October 2, 1994. Filed as Exhibit 3.1.2 to GTC's Annual Report on Form 10-K for the year ended December 28, 1997 (File No. 0-21794) filed on March 27, 1998 and incorporated by reference herein.
3.1.3	Articles of Amendment to the Restated Articles of Organization of GTC filed with the Secretary of the Commonwealth of Massachusetts on June 26, 1997. Filed as Exhibit 3 to GTC's Quarterly Report on Form 10-Q for the quarter ended June 29, 1997 (File No. 0-21794) filed on August 13, 1009 and incorporated by reference herein.
3.1.4	Articles of Amendment to the Restated Articles of Organization of GTC filed with the Secretary of the Commonwealth of Massachusetts on June 1, 2000. Filed as Exhibit 4.1.5 to GTC's Registration Statement on Form S-8 (File No. 333-38490) filed on June 2, 2000 and incorporated by reference herein.
3.1.5	Certificate of Vote of Directors Establishing a Series of a Class of Stock of GTC and designating the Series C Junior Participating Cumulative Preferred Stock. Filed as Exhibit 3.1 to GTC's Current Report on Form 8-K (File No. 0-21794) filed on June 1, 2001 and incorporated by reference herein.
3.1.6	Articles of Amendment to the Restated Articles of Organization of GTC filed with the Secretary of the Commonwealth of Massachusetts on May 31, 2002. Filed as Exhibit 3.1 to GTC's Current Report on Form 8-K (File No. 0-21794) filed on June 3, 3002 and incorporated by reference herein.
3.1.7	Articles of Amendment to the Restated Articles of Organization of GTC filed with the Secretary of the Commonwealth of Massachusetts on October 2, 2006. Filed as Exhibit 3.1 to GTC's Current Report on Form 8-K (File No. 0-21794) filed on October 5, 2006 and incorporated by reference herein.
3.1.8	Articles of Amendment to the Restated Articles of Organization of GTC filed with the Secretary of the Commonwealth of Massachusetts on December 11, 2006. Filed as Exhibit 3.8 to GTC's Annual Report on Form 10-K for the year ended December 31, 2006 (File No. 0-21794) filed on March 2, 2007 and incorporated by reference herein.
3.1.9	Articles of Amendment to the Restated Articles of Organization of GTC filed with the Secretary of the Commonwealth of Massachusetts on December 11, 2008. Filed as Exhibit 3.1 to GTC's Current Report on Form 8-K (File No. 0-21794) filed on December 16, 2008 and incorporated by reference herein.
3.2	By-Laws of GTC, as amended. Filed as Exhibit 3.1 to GTC's Quarterly Report on Form 10-Q for the quarter ended July 4, 1999 (File No. 0-21794) filed on August 18, 1999 and incorporated by reference herein.
4.1	Specimen Common Stock Certificate. Filed as Exhibit 4.1 to GTC's Registration Statement on Form S-1 (File No. 33-62782) and incorporated by reference herein.
4.2	Shareholder Rights Agreement, dated as of May 31, 2001, by and between GTC and American Stock Transfer and Trust Company, as Rights Agent. Filed as Exhibit 4.1 to GTC's Current Report on Form 8-K (File No. 0-21794) filed on June 1, 2001 and incorporated by reference herein.

4.2.1	Amendment No. 1 to Shareholder Rights Agreement, dated as of December 14, 2006, by and between GTC and American Stock Transfer and Trust Company. Filed as Exhibit 4.1 to GTC's Current Report on Form 8-K (File No. 0-21794) filed on December 20, 2006 and incorporated by reference herein.
4.2.2	Amendment No. 2 to Shareholder Rights Agreement dated as of December 22, 2008, by and between GTC and American Stock Transfer and Trust Company. Filed as Exhibit 4.1 to GTC's Current Report on Form 8-K (File No. 0-21794) filed on December 24, 2008 and incorporated by reference herein.
4.3	Warrant to Purchase Common Stock, dated November 12, 1999, issued to Genzyme Corporation. Filed as Exhibit 8 to Amendment No. 6 to Schedule 13D of Genzyme Corporation (File No. 005-46637) filed on November 24, 1999 and incorporated by reference herein.
4.4	Warrant to Purchase Common Stock, dated November 12, 1999, issued to Genzyme Corporation. Filed as Exhibit 9 to Amendment No. 6 to Schedule 13D of Genzyme Corporation (File No. 005-46637) filed on November 24, 1999 and incorporated by reference herein.
4.5	Registration Rights Agreement between GTC and certain Stockholders named therein dated March 20, 1998. Filed as Exhibit 10.53 to GTC's Annual Report on Form 10-K for the year ended December 28, 1997 (File No. 0-21794) filed on March 27, 1998 and incorporated by reference herein.
4.6	Form of Common Stock Purchase Warrant. Filed as Exhibit 10.3 to GTC's Current Report on Form 8-K (File No. 0-21794) filed on August 8, 2005 and incorporated by reference herein.
4.7	Form of Registration Rights Agreement. Filed as Exhibit 10.2 to GTC's Current Report on Form 8-K (File No. 0-21794) filed on August 8, 2005 and incorporated by reference herein.
4.8	Form of Common Stock Purchase Warrant. Filed as Exhibit 4.1 to GTC's Current Report on Form 8-K (File No. 0-21794) filed on December 12, 2005 and incorporated by reference herein.
4.9	Form of Common Stock Purchase Warrant. Filed as Exhibit 4.1 to GTC's Current Report on Form 8-K (File No. 0-21794) filed on July 20, 2006 and incorporated by reference herein.
4.10	Form of Subordinated Convertible Note issued to LFB Biotechnologies, S.A.S.U. Included as Exhibit B to the Stock and Note Purchase Agreement by and between GTC and LFB Biotechnologies, S.A.S.U. dated September 29, 2006, filed as Exhibit 10.1 to GTC's Current Report on Form 8-K (File No. 0-21794) filed October 5, 2006 and incorporated by reference herein.
4.11	Form of Common Stock Purchase Warrant. Filed as Exhibit 4.1 to GTC's Current Report on Form 8-K (File No. 0-21794) filed on February 8, 2008 and incorporated by reference herein.
4.12	Form of Common Stock Purchase Warrant. Filed as Exhibit 4.1 to GTC's Quarterly Report on Form 10-Q for the quarter ended June 29, 2008 (File No. 0-21794) filed on August 7, 2008 and incorporated by reference herein.
4.13	Form of Common Stock Purchase Warrant. Filed as Exhibit 4.2 to GTC's Quarterly Report on Form 10-Q for the quarter ended June 29, 2008 (File No. 0-21794) filed on August 7, 2008 and incorporated by reference herein.
4.14	Form of Secured Convertible Note issued to LFB Biotechnologies, S.A.S.U. Included as Exhibit A to the Note and Warrant Purchase Agreement by and between GTC Biotherapeutics, Inc. and LFB Biotechnologies S.A.S.U. dated October 31, 2008, filed as Exhibit 10.1 to GTC's Current Report on Form 8-K filed on November 6, 2008 (File No. 0-21794) and incorporated by reference herein.

4.15	Form of Common Stock Purchase Warrant issued to LFB Biotechnologies, S.A.S.U. Included as Exhibit B to the Note and Warrant Purchase Agreement by and between GTC Biotherapeutics, Inc. and LFB Biotechnologies S.A.S.U. dated October 31, 2008, filed as Exhibit 10.1 to GTC's Current Report on Form 8-K filed on November 6, 2008 (File No. 0-21794) and incorporated by reference herein.
10.1*	Agreement by and between GTC and Gene Pharming Europe B.V., dated as of September 21, 1994. Filed as Exhibit 10.49 to GTC's Registration Statement on Form S-1 (File No. 33-62782) and incorporated by reference herein.
10.2	Sublease Agreement by and between GTC and Genzyme Corporation, dated as of May 1, 1993. Filed as Exhibit 10.3 to GTC's Registration Statement on Form S-1(File No. 33-62782) and incorporated by reference herein.
10.3	License Agreement by and between GTC and Genzyme Corporation, as successor to IG Laboratories, Inc., dated as of May 1, 1993. Filed as Exhibit 10.4 to GTC's Registration Statement on Form S-1 (File No. 33-62782) and incorporated by reference herein.
10.4	Lease dated March 26, 1999 by and between GTC and NDNE 9/90 Corporate Center LLC. Filed as Exhibit 10.1 to GTC's Quarterly Report on Form 10-Q for the quarter ended July 4, 1999 (File No. 0-21794) filed on August 18, 1999 and incorporated by reference herein.
10.5	Hazardous Materials Indemnity Agreement by and between the GTC and Genzyme Corporation, dated December 28, 2998. Filed as Exhibit 10.28.5 to GTC's Annual Report on Form 10-K for the year ended January 2, 2000 (File No. 0-21794) filed on April 3, 2000 and incorporated by reference herein.
10.6*	License Agreement by and among GTC, Pharming Group N.V. and Pharming Intellectual Property B.V., dated June 21, 2002. Filed as Exhibit 10.3.1 to GTC's Quarterly Report on Form 10-Q for the quarter ended June 30, 2002 (File No. 0-21794) filed on August 2, 2002 and incorporated by reference herein.
10.7*	Amended and Restated License Agreement by and among Pharming Group, N.V. and Pharming Intellectual Property B.V. and GTC dated June 21, 2002. Filed as Exhibit 10.3.2 to GTC's Quarterly Report on Form 10-Q for the quarter ended June 30, 2002 (File No. 0-21794) filed on August 2, 2002 and incorporated by reference herein.
10.8*	Purchase Agreement by and between GTC and Genzyme Corporation, dated as of July 31, 2001. Filed as Exhibit 10.2 to GTC's Quarterly Report on Form 10-Q for the quarter ended September 30, 2001 (File No. 0-21794) filed on November 13, 2001 and incorporated by reference herein.
10.9*	Sublease Agreement by and between GTC and Antigenics, Inc., dated July 16, 2002. Filed as Exhibit 10.4 to GTC's Quarterly Report on Form 10-Q for the quarter ended June 30, 2002 (File No. 0-21794) filed on August 2, 2002 and incorporated by reference herein.
10.10	Amended and Restated Master Security Agreement by and between GTC and General Electric Capital Corporation, dated as of December 29, 2006. Filed as Exhibit 10.3 to GTC's Current Report on Form 8-K (File No. 0-21794) filed on January 4, 2007 and incorporated by reference herein.
10.10.1	Consent and Amendment No. 3 to Amended and Restated Master Security Agreement by and between GTC and General Electric Capital Corporation, dated as of December 22, 2008. Filed as Exhibit 10.4 to GTC's Current Report on Form 8-K (File No. 0-21794) filed on December 24, 2008 and incorporated by reference herein.

10.11	Promissory Note in the amount of $8 million by and between GTC and General Electric Capital Corporation, dated as of December 29, 2006. Filed as Exhibit 10.1 to GTC's Current Report on Form 8-K (File No. 0-21794) filed on January 4, 2007 and incorporated by reference herein.
10.12	Promissory Note in the amount of $2 million by and between GTC and General Electric Capital Corporation, dated as of December 29, 2006. Filed as Exhibit 10.2 to GTC's Current Report on Form 8-K (File No. 0-21794) filed on January 4, 2007 and incorporated by reference herein.
10.13*	Licensing and Supply Agreement by and between GTC and LEO Pharma A/S, dated as of October 31, 2005. Filed as Exhibit 10.1 to GTC's Current Report on Form 8-K/A (File No. 0-21794) filed on November 28, 2005 and incorporated by reference herein.
10.14**	GTC Amended and Restated 1993 Equity Incentive Plan. Filed as Exhibit 10.7 to GTC's Annual Report on Form 10-K for the year ended December 30, 2001 (File No. 0-21794) filed on March 22, 2002 and incorporated by reference herein.
10.15**	GTC Amended and Restated 2002 Equity Incentive Plan, as amended. Filed as Exhibit 10.1 to GTC's Current Report on Form 8-K (File No. 0-21794) filed on December 16, 2008 and incorporated by reference herein.
10.16**	GTC 2002 Employee Stock Purchase Plan. Filed as Exhibit 10.7 to GTC's Quarterly Report on Form 10-Q for the quarter ended March 31, 2002 (File No. 0-21794) filed on May 1, 2002 and incorporated by reference herein.
10.17	GTC Form of Confidential and Proprietary Information Agreement signed by GTC employees. Filed as Exhibit 10.9 to GTC's Registration Statement on Form S-1 (File No. 33-62782) and incorporated by reference herein.
10.18	GTC Form of Agreement Not to Compete. Filed as Exhibit 10.10 to GTC's Registration Statement on Form S-1 (File No. 33-62782) and incorporated by reference herein.
10.19	Form of Indemnification Agreement between GTC and its directors. Filed as Exhibit 10.12 to GTC's Annual Report on Form 10-K for the year ended December 31, 1994 (File No. 0-21794) and incorporated by reference herein. Such agreements are materially different only as to the signing directors and the dates of execution.
10.20**	Second Amended and Restated Employment Agreement, dated as of July 23, 2008, by and between GTC and John B. Green. Filed as Exhibit 10.4 to GTC's Quarterly Report on Form 10-Q for the quarter ending June 29, 2008 (File No. 0-21794) filed on August 7, 2008 and incorporated by reference herein.
10.21**	Amended and Restated Executive Employment Agreement, dated as of July 23, 2008, by and between GTC and Geoffrey F. Cox. Filed as Exhibit 10.3 to GTC's Quarterly Report on Form 10-Q for the quarter ending June 29, 2008 (File No. 0-21794) filed on August 7, 2008 and incorporated by reference herein.
10.22**	Management Agreement, dated as of July 23, 2008 by and between GTC and Harry Meade. Filed as Exhibit 10.5 to GTC's Quarterly Report on Form 10-Q for the quarter ending June 29, 2008 (File No. 0-21794) filed on August 7, 2008 and incorporated by reference herein.
10.23**	Amended and Restated Executive Change in Control Agreement, dated as of July 23, 2008, by and between GTC and Harry M. Meade. Filed as Exhibit 10.8 to GTC's Quarterly Report on Form 10-Q for the quarter ending June 29, 2008 (File No. 0-21794) filed on August 7, 2008 and incorporated by reference herein.

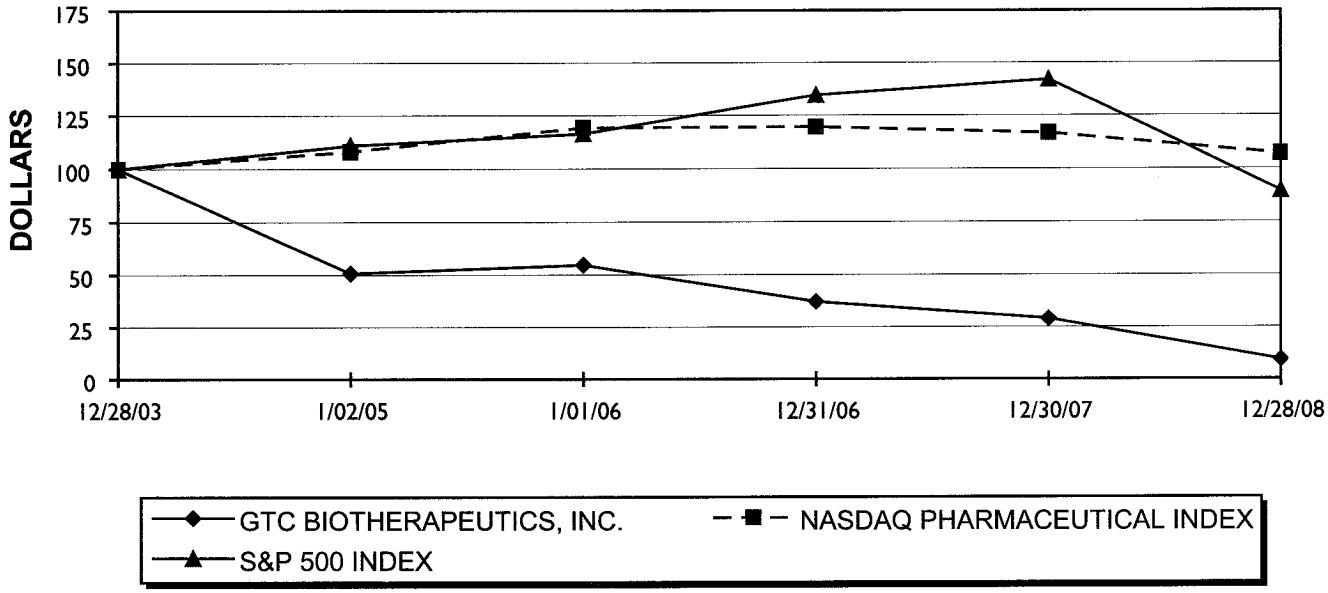
10.24**	Amended and Restated Management Agreement, dated as of July 23, 2008, by and between GTC and Daniel S. Woloshen. Filed as Exhibit 10.7 to GTC's Quarterly Report on Form 10-Q for the quarter ending June 29, 2008 (File No. 0-21794) filed on August 7, 2008 and incorporated by reference herein.
10.25**	Amended and Restated Executive Change in Control Agreement, dated as of July 23, 2008, by and between GTC and Daniel S. Woloshen. Filed as Exhibit 10.10 to GTC's Quarterly Report on Form 10-Q for the quarter ending June 29, 2008 (File No. 0-21794) filed on August 7, 2008 and incorporated by reference herein.
10.26**	Amended and Restated Management Agreement, dated as of July 23, 2008, by and between GTC and Richard A. Scotland. Filed as Exhibit 10.6 to GTC's Quarterly Report on Form 10-Q for the quarter ending June 29, 2008 (File No. 0-21794) filed on August 7, 2008 and incorporated by reference herein.
10.27**	Amended and Restated Executive Change in Control Agreement, dated as of July 23, 2008, by and between GTC and Richard A. Scotland. Filed as Exhibit 10.9 to GTC's Quarterly Report on Form 10-Q for the quarter ending June 29, 2008 (File No. 0-21794) filed on August 7, 2008 and incorporated by reference herein.
10.28*	Amended and Restated Joint Development and Commercialization Agreement dated June 30, 2008 by and between GTC and LFB Biotechnologies S.A.S.U. Filed as Exhibit 10.11 to GTC's Quarterly Report on Form 10-Q for the quarter ended June 29, 2008 (File No. 0-21794) filed on August 7, 2008 and incorporated by reference herein.
10.29	Stock and Note Purchase Agreement dated September 29, 2006, by and between GTC and LFB Biotechnologies S.A.S.U., including the form of convertible note attached as Exhibit B thereto. Filed as Exhibit 10.1 to GTC's Current Report on Form 8-K (File No. 0-21794) filed on October 5, 2006 and incorporated by reference herein.
10.29.1	Amendment No. 1 to Stock and Note Purchase Agreement dated October 18, 2006, by and between GTC and LFB Biotechnologies S.A.S.U. Filed as Exhibit 10.1 to GTC's Quarterly Report on Form 10-Q (File No. 0-21794) for the quarter ended March 30, 2008 filed on May 8, 2008 and incorporated by reference herein.
10.29.2	Amendment No. 2 to Stock and Note Purchase Agreement dated March 25, 2008, by and between GTC and LFB Biotechnologies S.A.S.U. Filed as Exhibit 10.2 to GTC's Quarterly Report on Form 10-Q (File No. 0-21794) for the quarter ended March 30, 2008 filed on May 8, 2008 and incorporated by reference herein.
10.30	Keepwell Agreement dated September 29, 2006, by and between GTC and Laboratories Francais du Fractionnement et des Biotechnologies S.A. Filed as Exhibit 10.2 to GTC's Current Report on Form 8-K (File No. 0-21794) filed on October 5, 2006 and incorporated by reference herein.
10.31	Form of Securities Purchase Agreement. Filed as Exhibit 10.2 to GTC's Current Report on Form 8-K (File No. 0-21794) filed on February 8, 2008 and incorporated by reference herein.
10.32*	Acquisition, Licensing, Development and Supply Agreement dated June 22, 2008 by and between GTC, ATIII LLC and Ovation Pharmaceuticals, Inc. Filed as Exhibit 10.1 to GTC's Quarterly Report on Form 10-Q for the quarter ending June 29, 2008 (File No. 0-21794) filed on August 7, 2008 and incorporated by reference herein.

10.33	Note and Warrant Purchase Agreement, dated as of October 31, 2008, by and between GTC and LFB Biotechnologies S.A.S.U., including the form of convertible note attached as Exhibit A thereto and the form of warrant attached as Exhibit B thereto. Filed as Exhibit 10.1 to GTC's Current Report on Form 8-K (File No. 0-21794) filed on November 6, 2008 and incorporated by reference herein.
10.34	Security Agreement, dated as of December 22, 2008, by GTC in favor of LFB Biotechnologies S.A.S.U. Filed as Exhibit 10.1 to GTC's Current Report on Form 8-K (File No. 0-21794) filed on December 24, 2008 and incorporated by reference herein.
10.35	Patent and License Security Agreement, dated as of December 22, 2008, by GTC in favor of LFB Biotechnologies S.A.S.U. Filed as Exhibit 10.2 to GTC's Current Report on Form 8-K (File No. 0-21794) filed on December 24, 2008 and incorporated by reference herein.
10.36	Trademark and License Security Agreement, dated as of December 22, 2008, by GTC in favor of LFB Biotechnologies S.A.S.U. Filed as Exhibit 10.3 to GTC's Current Report on Form 8-K (File No. 0-21794) filed on December 24, 2008 and incorporated by reference herein.
10.37	Patent and License Security Agreement, dated as of December 22, 2008, between GTC and General Electric Capital Corporation. Filed as Exhibit 10.5 to GTC's Current Report on Form 8-K (File No. 0-21794) filed on December 24, 2008 and incorporated by reference herein.
10.38	Trademark and License Security Agreement, dated as of December 22, 2008, between GTC and General Electric Capital Corporation. Filed as Exhibit 10.6 to GTC's Current Report on Form 8-K (File No. 0-21794) filed on December 24, 2008 and incorporated by reference herein.
10.39**	GTC 2008 Retention Incentive Plan. Filed as Exhibit 10.1 to GTC's Report on Form 8-K (File No. 0-21794) filed on July 3, 2008 and incorporated by reference herein.
10.40**	GTC December 2008 Retention Plan. Filed as Exhibit 10.2 to GTC's Current Report on Form 8-K (File No. 0-21794) filed on December 24, 2008 and incorporated by reference herein.
21	List of Subsidiaries. Filed herewith.
23	Consent of PricewaterhouseCoopers LLP. Filed herewith.
31.1	Certification of Chief Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. Filed herewith.
31.2	Certification of Chief Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. Filed herewith.
32	Certifications pursuant to 18 U.S.C. Section 1350. Filed herewith.

* Certain confidential information contained in the document has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended, or Rule 24b-2 promulgated under the Securities and Exchange Act of 1934, as amended.

** Indicates a management contract or compensatory plan.

Comparison of 5-Year Cumulative Total Return
Among GTC Biotherapeutics, Inc.,
S&P 500 Index and NASDAQ Pharmaceutical Index



Assumes $100 invested on Dec. 28, 2003
Assumes dividend reinvested
Fiscal year ending Dec. 28, 2008

Corporate Information

BOARD OF DIRECTORS

Geoffrey F. Cox, Ph.D.
Chairman of the Board
President and Chief Executive Officer
GTC Biotherapeutics, Inc.

Robert W. Baldridge
Independent Business Consultant
Former CEO and Director of
TSI Corporation

Kenneth A. Bauer, M.D.
Professor of Medicine
Harvard Medical School
Director Thrombosis Clinical Research
Beth Israel Deaconess Medical Center

Christian Béchon
Chairman and Chief Executive Officer
LFB Group

Francis J. Bullock, Ph.D.
Independent Consultant
Former Sr. Vice President of
Research Operations
Schering-Plough Research Institute

James A. Geraghty
Senior Vice President
Genzyme Corporation

Mary Ann Gray, Ph.D.
President
Gray Strategic Advisors, LLC

Michael J. Landine
Senior Vice President
Corporate Development
Alkermes, Inc.

Pamela W. McNamara
President
Cambridge Consultants, Inc.
Former CEO, CRF, Inc., Arthur D. Little

Marvin L. Miller
Former President and CEO of Nextran,
an affiliate of Baxter Healthcare
Corporation, and former Vice President
International of Johnson & Johnson

Alan W. Tuck
Partner
The Bridgespan Group,
a nonprofit consulting organization

EXECUTIVE OFFICERS

Geoffrey F. Cox, Ph.D.
Chairman of the Board
President and Chief Executive Officer
GTC Biotherapeutics, Inc.

John B. Green, C.P.A.
Senior Vice President
Chief Financial Officer and Treasurer
GTC Biotherapeutics, Inc.

Harry M. Meade, Ph.D.
Senior Vice President Research
and Development
GTC Biotherapeutics, Inc.

Richard A. Scotland
Senior Vice President Regulatory Affairs
GTC Biotherapeutics, Inc.

Daniel S. Woloshen
Senior Vice President and
General Counsel
GTC Biotherapeutics, Inc.

CORPORATE OFFICES

GTC Biotherapeutics, Inc.
175 Crossing Boulevard
Framingham, MA 01702
(508) 620-9700
www.gtc-bio.com

INDEPENDENT ACCOUNTANTS

PricewaterhouseCoopers LLP
Boston, MA

EXTERNAL LEGAL COUNSEL

Edwards Angell Palmer & Dodge LLP
Boston, MA

TRANSFER AGENT

American Stock Transfer
& Trust Company
59 Maiden Lane
New York, NY 10038
(800) 937-5449
www.amstock.com

The transfer agent is responsible for handling shareholder questions regarding lost stock certificates, address changes and changes of ownership or name in which shares are held.

MARKET FOR COMMON STOCK

Nasdaq Capital Market
Trading Symbol: GTCB

REPORT ON FORM 10-K

GTC's Annual Report on Form 10-K for the year ended December 28, 2008 is included herein. The report on Form 10-K and its accompanying exhibits are filed with the U.S. Securities and Exchange Commission and can be accessed in the SEC's EDGAR database (at www.sec.gov). Copies are available without charge upon written request to the Company at 175 Crossing Boulevard, Framingham, MA 01702, Attention: Tom Newberry or by calling Tom Newberry at (508) 620-9700 x5374

ANNUAL MEETING

The Annual Meeting of Shareholders is scheduled to be held on Wednesday, May 27, 2009 at 2:00 p.m. at the Forefront Center for Meetings and Conferences, 404 Wyman Street, Waltham, MA 02451

GTC Biotherapeutics, Inc.
175 Crossing Boulevard
Framingham, MA 01702
508-620-9700