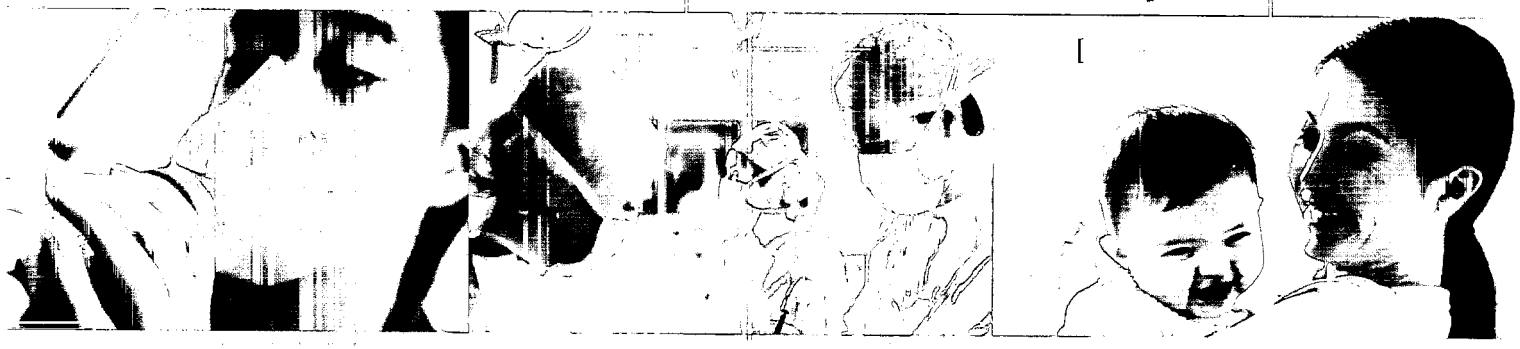
GTC Biotherapeutics, Inc.

Annual Report 2004



Dear Shareholders,

We reached an important milestone early in 2004 with the filing requesting marketing approval for ATryn® in Europe. ATryn®, our lead program, is a recombinant form of the human blood protein antithrombin. ATryn® has been studied for use in preventing deep vein thrombosis in patients with a hereditary antithrombin deficiency that are undergoing high risk procedures such as surgery or childbirth. We often refer to this as the HD indication. ATryn® is the first of what we envision as a pipeline of programs that seek to deliver a safe and assured supply of recombinant forms of therapeutic human plasma proteins.

ATryn® PROGRESS IN EUROPE AND THE US

At the time of this letter, we received a list of outstanding issues from the European Medicines Agency, or EMEA, during its review of our submittal. We will need to resolve these issues to obtain approval to market ATryn® in Europe.

ATryn® has also begun a parallel journey in the US to be considered for use in the same HD indication. We filed an amended Investigational New Drug application with the FDA in late December 2004. This filing seeks permission for a clinical study with the potential, assuming a successful conclusion, to form a basis for a request for approval. We are planning to initiate this study in the second quarter of 2005 and we expect enrollment of patients to take approximately one year.

Based on previous research papers, we believe that there are approximately 80,000 people in the European Union and 60,000 people in the US with the HD condition. There has been very little plasma-derived antithrombin sold in the US partly due to its limited availability from a single supplier. Establishing a robust supply of recombinant product in the US is a significant market opportunity. We also believe significant opportunities exist for ATryn® in larger market indications resulting from acquired deficiencies, such as in the treatment of severe burns. These opportunities can be accessed through further clinical development. We believe that development of these opportunities presents ATryn® with the potential to build a market of $500 million to $700 million annually worldwide.

As we move the regulatory process forward, we will continue discussions with a number of potential marketing and development partners for ATryn® in Europe and the US. In addition, we continue to explore the

GTC Biotherapeutics is a leader in the development, production and commercialization of therapeutic proteins through transgenic animal technology.

option of establishing our own small sales force, either internally or through a contract sales organization. If we determine that one or more companies represent the best partnering arrangement, we may supplement this commercial capability with our own sales force for countries where the regional partners do not have a presence.

ADDITIONAL RECOMBINANT PLASMA PROTEINS

We continue to evaluate the process capability and capacity to support the development of markets for recombinant human albumin, or rhA, as an excipient and as a component in cell culture media. An excipient is a stabilizing agent of a biologic drug formulation. Starting in the second half of 2004, we began providing samples of rhA to potential customers for evaluation. In 2005, we will continue to evaluate the business opportunities for this program.

A third recombinant plasma protein in our internal pipeline is a recombinant form of human alpha-1 antitrypsin, or AAT. There are an estimated 3.4 million individuals worldwide afflicted with AAT deficiency. This genetic condition can lead to emphysema for which AAT, derived from the human blood supply, is currently used as a chronic treatment. We also believe that our recombinant AAT product, or rhAAT, may hold therapeutic value in treating cystic fibrosis, chronic obstructive pulmonary disease, acute respiratory distress syndrome, and severe asthma. Like antithrombin and albumin, the AAT protein is difficult to express at economically viable quantities in traditional recombinant production systems. As with the first two programs, we believe that the well-characterized nature and expandable source of supply of rhAAT offers market advantages. These advantages may allow us to penetrate the existing sales of the plasma-derived product and through clinical trials that lead to approval to enter expanded markets.

With ATryn®, rhA, and rhAAT, we are on the path towards developing a strategic position in recombinant plasma proteins. We are following the business model of offering a safe, highly pure, and unconstrained supply of these known chemical entities to establish valuable therapeutic markets that expand upon the traditional plasma-based business. This business model has already been demonstrated by other companies for the recombinant blood factors, VIIa, VIII, and IX. The blood factors are among the few proteins found in human plasma that can be expressed at reasonable levels in traditional recombinant production systems. The total sales for all

GTC Biotherapeutics Board of Directors from left to right: Francis J. Bullock, Ph.D., Marvin L. Miller, Robert W. Baldridge, Geoffrey F. Cox, Ph.D., Pamela W. McNamara, Michael J. Landine (back), Kenneth A. Bauer, M.D. (front), James A. Geraghty and Alan W. Tuck

of these recombinant products is now about $3 billion compared to the approximately $1 billion of sales achieved by the plasma-derived products.

PROGRESS WITH PARTNERSHIPS

I am pleased to report we made significant progress in 2004 in advancing the programs in our external portfolio of partnerships towards production for clinical trials. We are providing purified material to Merrimack Pharmaceuticals for its clinical program with its MM-093 product, a recombinant human alpha feto-protein (AFP). AFP is also a difficult to express blood protein, but one that is not derived from the fractionated human blood supply since it is normally only present in significant quantities during pregnancy. Merrimack is in Phase II studies of MM-093. We also have a program with Centocor for an undisclosed protein. In 2004, on behalf of Centocor, we produced material for extended preclinical studies. We anticipate herd expansion later this year to prepare for clinical production, assuming success of the preclinical studies.

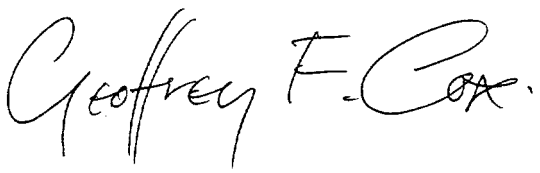
DRIVEN AND ENABLED BY PEOPLE

I am also pleased to welcome two new board members to GTC, Kenneth Bauer, M.D. and Michael Landine. Both of these new directors have important experience and bring new perspectives to our business. Dr. Bauer is an internationally recognized authority in the field of thrombosis and haemostasis, providing a strong understanding of the clinical aspects of both ATryn® and our other recombinant blood protein programs. Michael Landine has played an important role in the development of Alkermes over many years and will bring significant experience to GTC, particularly in the areas of finance and corporate development.

Our progress in 2004 has been driven by the extraordinary dedication and skill of our employees. They have risen to the challenge of leading the industry in entering the first regulatory review of a transgenically produced product in the US or Europe. This is a process which demands painstaking attention to detail and careful development of professional relationships across many functions both inside and external to GTC. I also want to thank our employees for achieving our objectives while meeting the Securities and Exchange Commission requirements resulting from the Sarbanes-Oxley legislation. While many of these accomplishments do not make it into the spotlight of news events, the expertise which our employees bring to these obligations is essential to position GTC for continued growth.

I thank all of our investors for their support of GTC. Together, we can look forward to continuing our progress to establishing GTC as a commercial products company.

Sincerely,



Geoffrey F. Cox, Ph.D.

Achieving a Regulatory Milestone

In January 2004, GTC submitted its request for market authorization in Europe for ATryn® as a prophylactic treatment of hereditary antithrombin deficiency (HD) during high-risk situations such as surgery and childbirth. We have received a list of outstanding issues from the European Medicines Agency, or EMEA, during its review of our submittal. We also submitted an amended IND to the FDA to perform a pivotal HD clinical study for ATryn® in the United States. We are planning to initiate this study in 2005 and we expect patient enrollment to take approximately one year.

Our submission in Europe was a milestone event for GTC, as it was the first program we have submitted to a regulatory agency for review. It was also the first recombinant protein produced using transgenic technology to be submitted to any regulatory agency in the United States or Europe.

Antithrombin is a plasma protein with anticoagulant and anti-inflammatory properties. We have developed goats that have the human antithrombin gene linked to a milk-protein promoting gene, expressing this protein in their milk. This transgenic approach provides the opportunity to produce recombinant forms of proteins, such as antithrombin, that are difficult to express in economically viable quantities in conventional production systems.

CLINICAL OPPORTUNITIES FOR ATryn®

Anticoagulant Properties

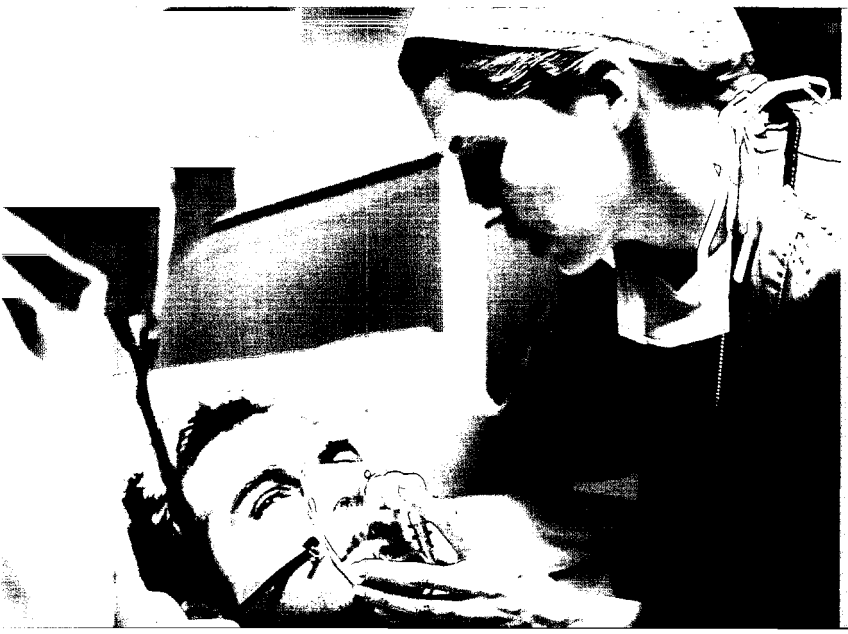
- HEREDITARY DEFICIENCY (HD)
- ACUTE LYMPHOCYTIC LEUKEMIA
- DISSEMINATED INTRAVASCULAR COAGULATION (DIC)
- CORONARY ARTERY BYPASS GRAFTING – HEPARIN RESISTANCE (CABG-HR)

Both Properties

- BURNS
- NEUROCOGNITIVE IMPAIRMENT ASSOCIATED WITH CARDIOPULMONARY BYPASS (CABG-COG)
- TRAUMA
- VENO-OCCLUSIVE DISEASE (VOD)
- SEPSIS

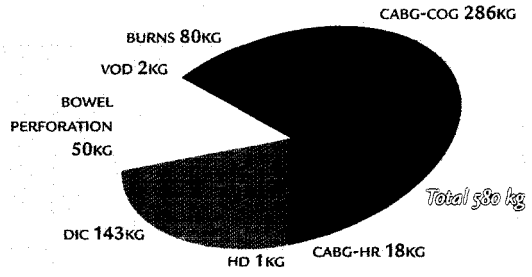
Anti-Inflammatory Properties

- BOWEL PERFORATION
- INHALATION INJURY



ESTIMATED POTENTIAL ANNUAL USES FOR ATryn® IN THE UNITED STATES*

Estimated potential capacity of antithrombin (AT) from US plasma sources is 100 kg (8 million donors[§] → 14 million units whole blood → 2 million liters plasma → 100 kg AT)

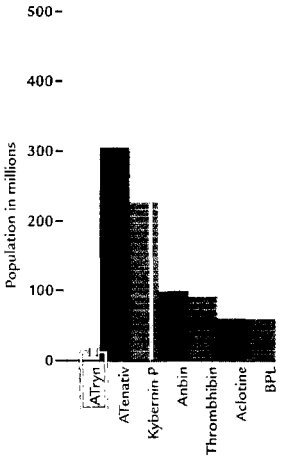


*Assuming appropriate clinical development and regulatory approvals
§American Association of Blood Banks

Until now, the availability of antithrombin for therapeutic use has been dependent on a process which fractionates human plasma into multiple components. Production of antithrombin using this method is highly dependent on the availability and quality of human donor blood sources. Worldwide supply is also hindered by the inability to pool donor blood between major demographic areas such as Europe and the United States due to human viral safety profiles. Even within Europe, different blood plasma-derived antithrombin products may be available on a country-by-country basis. Antithrombin is one of many blood proteins that have been difficult to express commercially at economically viable quantities using conventional recombinant production systems. ATryn® has the potential to be the first recombinant antithrombin to offer an unconstrained supply.

TOTAL POPULATION WHERE ANTITHROMBIN PRODUCTS ARE AVAILABLE IN EUROPE

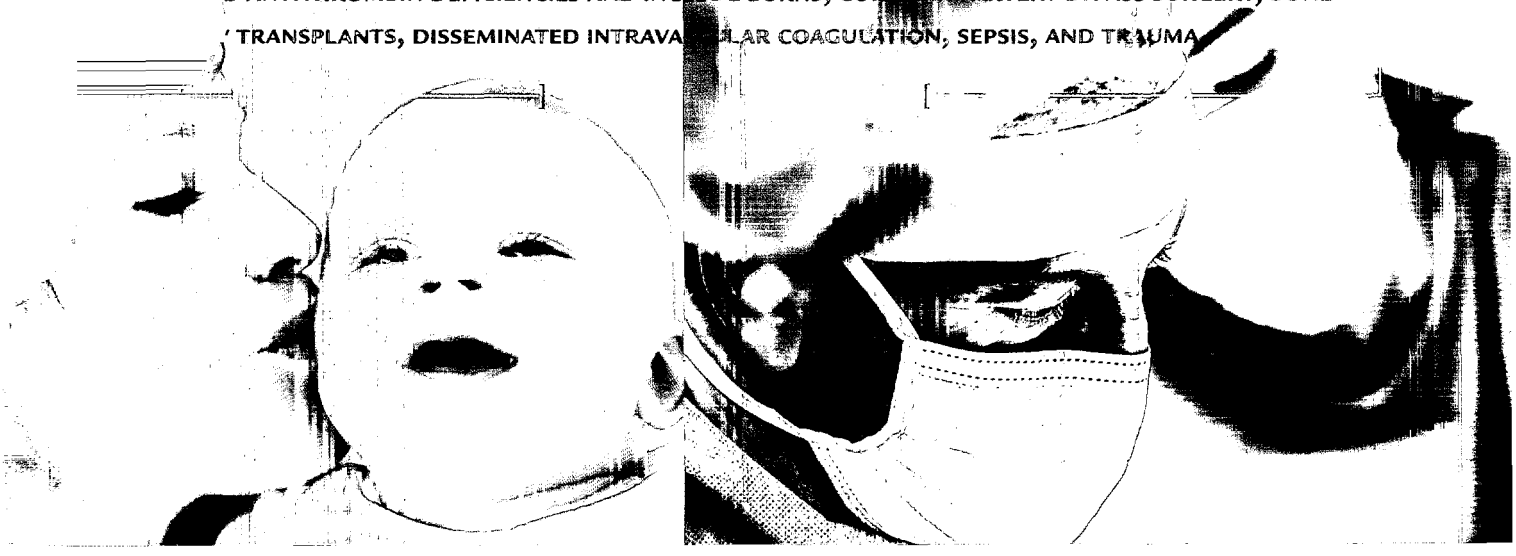
Approval of ATryn® would make recombinant antithrombin available to the entire European Union compared to the plasma-derived antithrombin products that are currently sold in various European countries.



Source: Martindale: The Complete Drug Reference, Census data

PENETRATING AN UNDERSERVED MARKET

WE BELIEVE THAT THERE IS AN OPPORTUNITY TO DEVELOP A $500 MILLION TO $700 MILLION ANNUAL MARKET FOR ATRYN® WORLDWIDE. THIS MARKET WILL BE DEVELOPED BY PROVIDING A SAFE AND WELL-CHARACTERIZED PRODUCT TO PENETRATE THE APPROXIMATELY $250 MILLION MARKET THAT CURRENTLY EXISTS FOR PLASMA-DERIVED ANTITHROMBIN OUTSIDE THE US, ESTABLISHING A ROBUST ANTITHROMBIN MARKET IN THE US WITH OUR UNCONSTRAINED SUPPLY, AND EXPANDING THE OVERALL MARKET THROUGH CLINICAL DEVELOPMENT OF NEW INDICATIONS. THESE POTENTIAL INDICATIONS ALL RELATE TO D ANTITHROMBIN DEFICIENCIES AND INCLUDE BURNS, CORONARY ARTERY BYPASS SURGERY, BONE TRANSPLANTS, DISSEMINATED INTRAVASCULAR COAGULATION, SEPSIS, AND TRAUMA.



Expanding a Pipeline of Recombinant Plasma Proteins

Historically, production of plasma proteins for therapeutic use has relied on the availability and fractionation of donated human blood plasma. Although some plasma proteins are now available in recombinant forms, most have been found to be difficult to express at economically viable levels using conventional production systems.

We currently have three recombinant blood proteins in our internal program portfolio. ATryn®, as described earlier in this report, is being reviewed for marketing authorization approval in Europe. The second product is recombinant human albumin (rhA) and the third is recombinant human alpha-1 antitrypsin (rhAAT).

RECOMBINANT HUMAN ALBUMIN – rhA

We have produced qualification batches of rhA and have sampled potential customers. Some of these customers are evaluating the use of our rhA product as an excipient. When used as an excipient, albumin functions to stabilize the active biologic ingredient in a drug formulation. Other customers are considering rhA as a replacement for bovine serum albumin, which is used as a nutrient component in many commercial cell culture manufacturing processes. In the longer term, we remain interested in entering the therapeutic blood expander market that represents the bulk of plasma-based albumin sales currently.

RECOMBINANT HUMAN ALPHA-1 ANTITRYPSIN – rhAAT

In our rhAAT program, we are in the process of establishing clinical, regulatory, and commercial development strategies. Hereditary AAT deficiency can lead to emphysema. The plasma-derived products are used as a chronic treatment for this disease.

MAJOR PLASMA PRODUCT MARKETS*

Dollars in thousands

Product	Recombinant	Plasma derived	Totals
Factor VIII	$2,000	$ 850	$2,850
Factor VIIa	650	–	650
Factor IX	250	200	450
Antithrombin	IN REVIEW	200	200
Albumin	–	550	550
AAT	–	250	250
IVIG	–	2,100	2,100
Other§	–	550	550
Totals	$2,900	$4,700	$7,600

*M. Cooke, K. Nuske, Goldman Sachs JBWere analyst report, April 2004

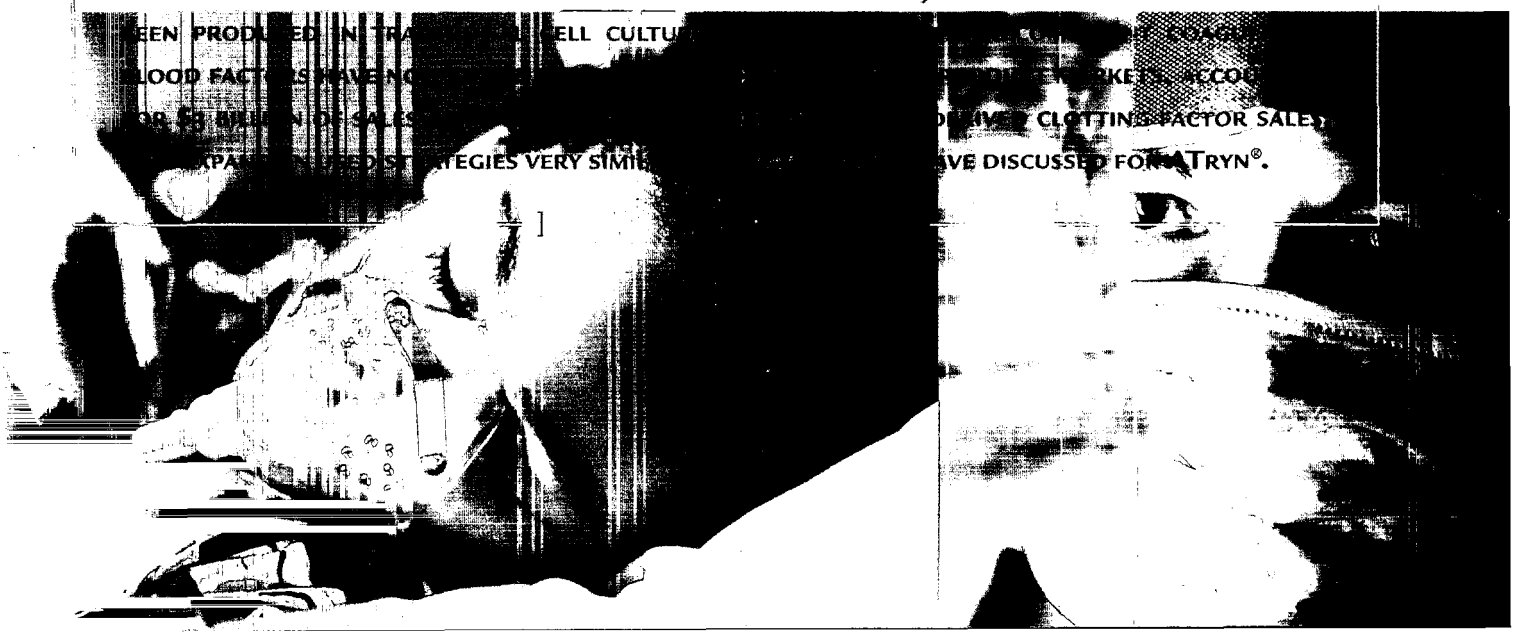
§ Sealants and Rho-D Ig

AAT deficiency is one of the most common serious hereditary disorders, with approximately 3.4 million people affected worldwide. Clinical research suggests that rhAAT therapy may also be beneficial to cystic fibrosis patients. In addition, we believe that rhAAT is a potential treatment for a number of pulmonary conditions, including chronic obstructive pulmonary disease, acute respiratory distress syndrome, and severe asthma.

In February 2005, GTC completed a licensing agreement with Eric F. Bernstein, M.D., a dermatologic laser surgeon and researcher in skin aging. This licensing agreement will aid Dr. Bernstein in his development of rhAAT for dermatological applications, including the potential to treat the effects of photoaging. Accumulation of abnormal elastic tissue, called 'solar elastosis', is the main change in the deeper layers of photoaged skin. Research suggests rhAAT interferes with elastin breakdown, the first part in the process of destroying the normal elastin of photoaged skin, and may delay the associated changes.

DEVELOPING A STRATEGIC POSITION

WE ARE ON THE PATH TOWARDS DEVELOPING A STRATEGIC POSITION IN RECOMBINANT PLASMA PROTEINS AND FOLLOWING THE BUSINESS MODEL OF OFFERING A SAFE, HIGHLY PURE, AND UNCONSTRAINED SUPPLY OF THESE KNOWN CHEMICAL ENTITIES TO ESTABLISH VALUABLE THERAPEUTIC MARKETS THAT EXPAND UPON THE TRADITIONAL, PLASMA-BASED BUSINESS. THIS HAS ALREADY BEEN DEMONSTRATED IN THE MARKETPLACE WITH THE RECOMBINANT COAGULATION BLOOD FACTORS VIIa, VIII AND IX THAT CAN AND HAVE



Selected Financial Data

(Dollars in thousands except per share data)

	For the Fiscal Years Ended				
	January 2, 2005	**December 28, 2003**	**December 29, 2002**	**December 30, 2001**	**December 31, 2000**
Statement of Operations Data[1]					
Net Revenues	**$ 6,626**	$ 9,764	$ 10,379	$ 13,740	$ 16,163
Operating costs and expenses	**35,819**	40,081	36,288	37,584	32,749
Operating loss from continuing operations	**(29,193)**	(30,317)	(25,909)	(23,844)	(16,586)
Loss from continuing operations	**(29,493)**	(29,537)	(24,320)	(18,792)	(13,817)
Loss from discontinued operations	**–**	–	–	–	(324)
Gain from sale of discontinued operations	**–**	–	–	2,236	–
Net loss available to common shareholders	**(29,493)**	(29,537)	(24,320)	(16,556)	(14,215)
Net loss available per common share	**(0.79)**	(1.00)	(0.86)	(0.55)	(0.50)
Weighted average number of shares *outstanding (basic and diluted)*	**37,360,758**	29,562,152	28,353,490	29,975,167	28,373,283
Balance Sheet Data[1]					
Cash and cash equivalents	**$ 1,835**	$ 5,733	$ 26,911	$ 26,850	$ 41,024
Marketable securities	**20,446**	25,358	30,438	63,598	25,508
Working capital	**10,639**	23,967	47,682	74,458	88,389
Net assets of discontinued contract research operations held for sale	–	–	–	–	37,272
Total assets	**57,301**	71,072	95,373	120,443	134,403
Long-term liabilities	**9,336**	12,582	12,823	80	294
Shareholders' equity	**33,653**	48,161	68,772	101,950	114,843

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

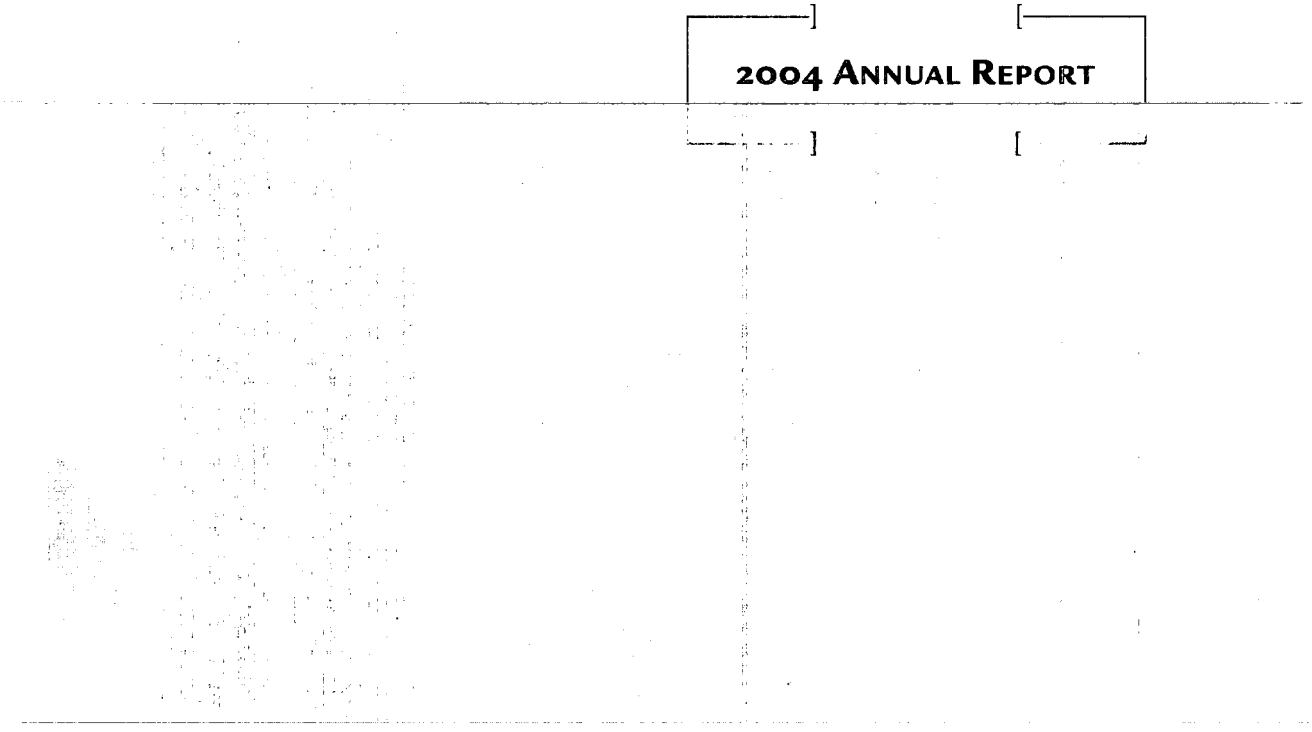
[1] For all periods presented, the net results and assets of Primedica Corporation are shown as discontinued operations. Primedica was sold in February 2001.

Important Note to Investors

This document contains forward-looking information, including statements about research and development programs and the potential size of the markets for GTC Biotherapeutics' products and services. Actual results may differ materially from these statements because of a number of factors, including market acceptance of the Company's products and services; content and timing of decisions made by the U.S. Food and Drug Administration and other regulatory agencies; the accuracy of the Company's information about competitors, potential competitors, market sizes and the price-sensitivity of customers; and the Company's ability to obtain patents, to obtain adequate funding for research and development programs, and to recruit and retain adequate numbers of qualified employees. These and other risk factors are described or referenced to in more detail in the Company's most recent 10-K filed with the Securities and Exchange Commission.

Form 10-K

[For the fiscal year ended January 2, 2005]



SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-K

FOR ANNUAL AND TRANSITION REPORTS PURSUANT TO SECTIONS 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

(Mark One)

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

For the fiscal year ended January 2, 2005

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:
None

Securities registered pursuant to Section 12(g) of the Act:
Common Stock, par value $0.01
Rights to Purchase Series C Junior Participating Cumulative Preferred Stock, par value $0.01 per share
(Title of each class)

Indicate by check mark whether the Registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding twelve months 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 an accelerated filer (as defined in Exchange Act Rule 12b-2). Yes ☒ No ☐

Aggregate market value of voting stock held by non-affiliates of the Registrant as of July 4, 2004, the last business day of the Registrant's most recently completed second fiscal quarter, was approximately $61,920,405, based on the closing sale price of the Company's Common Stock as reported on the NASDAQ National Market.

Number of shares of the Registrant's Common Stock outstanding as of March 1, 2005: 46,658,728

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's Proxy Statement for the Annual Meeting of Stockholders to be held May 25, 2005 are incorporated by reference into Part III of this Form 10-K.

PART I

In this Annual Report on Form 10-K, the words "we", "our", "ours" and "us" refer only to GTC Biotherapeutics, Inc. and not to any other person or entity.

Notes Regarding Forward-Looking Statements

This Annual Report on Form 10-K 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" within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act") and Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), as enacted by the Private Securities Litigation Reform Act of 1995. 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, regulatory review of our ATryn® product, our ability to enter into transgenic research and development collaborations in the future and the terms of such collaborations, the results of research and development and preclinical and clinical testing of our internal products, competitive and technological advances and regulatory requirements, and those set forth in Exhibit 99 "Important Factors Regarding Forward-Looking Statements" to this Form 10-K, which is incorporated into this item by this reference.

ITEM 1. BUSINESS

Overview

We are a leader in the development and production of human therapeutic proteins through transgenic technology. We are focusing our pipeline of internal product programs on recombinant forms of proteins that are currently derived from human blood plasma, for therapeutic uses. Our lead product candidate, a recombinant form of human antithrombin known as ATryn®, is undergoing review for market authorization in Europe. We believe ATryn® is the first protein produced by transgenic technology to undergo review for market authorization in the U.S. or Europe.

Using our transgenic technology we insert protein-specific DNA into an animal to enable it to produce that specific protein in its milk. We then purify the protein from the milk to obtain the therapeutic product, which is typically administered by injection. We use this technology to focus on those potential therapeutic proteins that are either difficult to express in traditional bioreactor-based technologies, or for those product candidates where the commercial volumes require significant capital investment for production capacity using conventional methods. Human blood proteins that are used for therapeutics may have either or both of these characteristics.

We have three recombinant blood proteins in active development in our internal pipeline:

- **ATryn:** We have completed several steps in the review process of our Market Authorization Application, or MAA, to the European Medicines Agency, or EMEA, for the use of ATryn® in patients with a hereditary antithrombin deficiency who are undergoing high risk procedures such as surgery or childbirth. We anticipate the EMEA's opinion on the MAA in the first half of 2005, with the potential for full approval in mid-2005, followed by the initiation of commercial sales.
- **rhA:** We have begun producing qualification batches of recombinant human albumin, or rhA, and providing samples to potential customers for evaluations in cell culture applications and as a stabilizer, or excipient, of active biologic ingredients in drug formulations. Albumin sourced from the human blood supply is currently being used as an excipient, while other forms of albumin, primarily from bovine sources, have been used as part of the nutrient media used in cell culture systems.
- **rhAAT:** We have developed goats which produce our third recombinant blood protein currently in development known as rhAAT, which is a recombinant form of human alpha-1 antitrypsin. Hereditary deficiency of alpha-1 antitrypsin may lead to the onset of emphysema.

We believe that the commercial marketplace will value recombinant forms of therapeutic human blood proteins that are currently derived from the liquid portion of the blood, or plasma, and that our transgenic approach is uniquely able to offer

unlimited and well characterized sources of supply. Our belief in the market value of plasma proteins is based, in part, on the sales experience of recombinant forms of the blood clotting plasma proteins known as factors VII, VIII, and IX. Unlike other plasma proteins, these recombinant clotting factors can be produced commercially in traditional technologies and have generated $3 billion of sales worldwide compared to the $1 billion of sales worldwide for plasma-sourced clotting factor products. Our platform technology may be able to replicate this experience in a broad array of other blood proteins. The therapeutic blood protein market, excluding the products focused on the treatment of hepatitis, currently generates approximately $7 billion of sales.

We are also developing two additional internal programs, a malaria vaccine in a program fully funded by the National Institute of Allergy and Infections Diseases, or NIAID, and an agonistic antibody to CD-137 licensed from the Mayo Clinic under a Flexible System to Advance Innovative Research grant, or FLAIR grant, funded by the National Cancer Institute, or NCI.

In addition to our internal programs, we are using our transgenic technology platform in a portfolio of external programs for the development of transgenic production to supply clinical and eventually commercial material for our partners. The most advanced external program is with Merrimack Pharmaceuticals, Inc. for transgenic production and purification of Merrimack's recombinant human alpha-fetoprotein, known as MM-093, which is also a human blood protein. Our transgenically produced version of MM-093 is one that Merrimack has used in its Phase I and Phase II human clinical studies as it evaluates the compound and its requirements for further trials. MM-093 has been difficult to express in traditional recombinant protein production systems. We are also working with Centocor Inc. to develop transgenic protein production for an undisclosed protein. We have supplied product to Centocor for preclinical evaluation.

We are dependent upon funding from equity financings, partnering programs and proceeds from short and long-term debt to finance operations until such time product sales and royalties occur and we achieve positive cash flow from operations. Our partnering initiatives include licensing and development agreements with collaborative partners for the development, production and purification of transgenically produced forms of therapeutic recombinant proteins. The terms of the agreements typically include non-refundable license fees, funding of research and development, payments based upon the achievement of certain milestones, revenue from sales of product to partners, and royalties on future product sales, if any.

Internal Programs

Recombinant Human Antithrombin (ATryn®)

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 economically viable levels in traditional recombinant production systems. In late 2001, we were granted permission by the EMEA to conduct clinical studies of ATryn®, our recombinant form of human antithrombin, in individuals who express a low level of antithrombin in their blood as a result of a hereditary deficiency of antithrombin, referred to as HD. There are approximately 1 in 5,000 people with HD representing approximately 60,000 people in the U.S. and approximately 80,000 in Europe. In December 2001, we began dosing HD patients in a pharmacokinetic study to establish an appropriate dosing regimen for a subsequent efficacy study. A pharmacokinetic study is the study of the bodily absorption, distribution, metabolism, and excretion of drugs. We successfully completed this 15 patient study and began an efficacy study in HD patients in 2002, primarily based in Europe but also including patients in the United States. The efficacy study was designed to assess the prevention of deep vein thromboses, or DVT, among HD patients that are undergoing surgery or childbirth.

Based on EMEA guidance, at least 12 evaluable patients were required to be included in the efficacy study. We enrolled a total of 14 patients. Our Market Authorization Application, or MAA, which was submitted to the EMEA in January 2004, includes data from this trial, as well as data from patients treated under a compassionate use program. The EMEA has accepted the MAA for review and will make a determination of the safety and efficacy of ATryn® and assess whether the product is approvable for commercial sale. We believe that ATryn® is the first transgenically produced therapeutic protein to be considered for approval by a regulatory agency in the U.S. or Europe. We have also filed an amended Investigational New Drug, or IND, application with the U.S. Food and Drug Administration, or FDA, to authorize a further clinical study in the HD indication that, together with the data package used in the European submittal, is intended to form the basis for approval of ATryn® in the U.S. We anticipate starting this U.S. trial in the first half of 2005 and completing it in 2006.

We are in discussions with prospective partners with the potential of providing financial, sales and marketing support for the ATryn® program in Europe in addition to support for clinical development. We are also considering the option of establishing a limited sales force to support commercial sales of ATryn® for the HD indication, following approval for sale in Europe. This sales force could be developed internally or may be initiated through a contract sales organization. We plan to expand ATryn®'s market opportunity through one or more clinical studies in order to develop additional potential acquired

deficiency indications. We plan to produce more ATryn® in 2005 for commercial supply and to prepare for the initiation of clinical studies in a larger acquired deficiency indication in 2006. Acquired antithrombin deficiency occurs in a number of conditions, and may result from a decrease in the amount of antithrombin produced, an increase in the rate of antithrombin consumed or an abnormal loss of antithrombin in the circulatory system. Examples of these conditions are burns, heparin resistance, patients undergoing surgery which requires cardiopulmonary bypass, trauma, acute liver failure, disseminated intravascular coagulation, sepsis and septic shock, multiple organ failure, pre-eclampsia and bone marrow or organ transplantation.

Our plan is to develop an expanded market for ATryn® through additional product indication approvals and by removing limitations of supply. If we develop ATryn® for expanded clinical indications we believe the product will have a worldwide market potential of $500 - $700 million. The existing worldwide sales for plasma-derived antithrombin is estimated to be approximately $250 million, of which less than $10 million is sold in the U.S. due to the limited availability from a single supplier.

Recombinant Human Albumin (rhA)

Albumin is a plasma protein that is principally responsible for maintaining the osmotic pressure in the vascular system, as well as maintaining plasma volume and the balance of fluids in blood. It is critical to the transport of amino acids, fatty acids and hormones in the blood stream. Albumin is principally used therapeutically as a blood volume expander in situations of blood loss and/or decreased blood albumin levels which can result from shock, serious burns, pre- and post-operative conditions, congestive heart failure and gastric, liver and intestinal malfunctions. Albumin is also used as a non-active stabilizer, or excipient, for the active ingredient in biologic drug formulations. Human serum albumin and bovine serum albumin may also be used in the media for cell cultures, both as part of *in vitro* fertilization as well as in bioreactor production systems.

Our strategy is to first develop our recombinant form of human albumin, or rhA, in the excipient or cell culture applications where there is the potential for commercial sales sooner than is practical in the blood expander indication and with significantly lower capital investment. We believe that the recombinant nature of this product can lead to a well characterized protein and a stable single source of supply. This will provide drug manufacturers the opportunity to avoid human plasma-derived albumin as an excipient for their recombinant products and establish a universally acceptable supply. We believe this will allow rhA to make substantial penetration into the existing excipient market. During 2004, we initiated the production of qualification batches for evaluation by potential customers. These customer evaluations are for the excipient, cell culture and *in vitro* fertilization markets. We anticipate that commercial sales of rhA in the excipient market will require some clinical evaluation, primarily to assess safety, and the development of a Drug Master File to support end user regulatory filings. We believe that under this timetable for development we have the opportunity to achieve commercial sales of rhA within two to three years, depending primarily on the level of development funding devoted to this program. The timetable of development will be dependent upon our financial resources, as well as our ability to attract marketing or strategic partners to provide additional funding.

rhA is another example of a difficult-to-express plasma protein which is also required in large volumes. We estimate that about $150 million to $200 million of the market total is sold for excipient and cell culture use. We estimate the total production volume to meet the needs of the excipient market is in the range of one to two metric tons per year. We are developing this program in transgenic cattle that are maintained by TransOva Genetics in Iowa.

In late 2002, we restructured our relationship with Fresenius AG into a joint venture referred to as the Taurus Joint Venture, which is managing the development of the rhA program. We currently have approximately a 57% interest in the joint venture. The joint venture structure provides the flexibility to attract additional marketing or strategic partners that may also assist with the financing of the program. We are engaged in ongoing discussions with potential partners. Ownership interests will be adjusted based on future levels of financial support provided by existing and new partners. Fresenius has not contributed new financing since the formation of the Taurus Joint Venture. Currently, we are developing the rhA program using our existing resources under an extended timetable, until there is additional financing.

The existence of the Taurus Joint Venture is perpetual unless terminated or dissolved earlier in accordance with the terms of the agreement. Upon any liquidation, sale or other disposition of all or substantially all of the assets of the Taurus Joint Venture, and after the payment of debts and liabilities, expenses of liquidation and any reserves for unforeseen liabilities or in-kind distributions, the net proceeds would be applied and distributed first to Fresenius and then to us, according to our respective percentage interests. Each member would also have reversion rights to any intellectual property it contributed to the Taurus Joint Venture. We consolidate the Taurus Joint Venture on our financial statements for financial reporting purposes.

Recombinant Alpha-1 Antitrypsin (rhAAT)

We have begun development of recombinant human alpha-1 antitrypsin, or rhAAT, which, like antithrombin and albumin, is a product that is currently available from fractionated human plasma. Plasma-derived AAT products generate worldwide sales of about $250 million. We believe that our recombinant form of alpha-1 antitrypsin, or AAT, can provide a highly pure and unconstrained supply to the market. AAT is currently used to treat the congenital deficiency of this protein which can lead to emphysema. AAT supplementation using pulmonary delivery has also been considered as a therapeutic approach in the treatment of cystic fibrosis and we believe that rhAAT may also have the potential as a treatment for acute respiratory distress syndrome, chronic obstructive pulmonary disease, and severe asthma. Similar to many other plasma proteins, AAT is difficult to express in traditional recombinant production systems in economically viable quantities.

We have developed goats that produce rhAAT. We have also developed a bench scale purification process and are in the process of defining the clinical and regulatory program for this product. The level and speed of development of this product will be dependent upon our financial resources.

We recently entered into a licensing agreement for rights to the limited topical use of rhAAT in cosmetic applications.

Malaria Vaccine

We are developing a recombinant form of a malaria surface protein known as MSP-1, which is normally expressed by the malaria parasite, for use as an antigen in a malaria vaccine. Malaria is a disease that has an annual incidence in more than 300 million people worldwide and results in several million deaths annually, primarily among children. We have been working with the National Institutes of Health, or NIH, and the Federal Malaria Vaccine Coordinating Committee to develop transgenic production of the MSP-1 protein as an antigen for a vaccine and to examine the options for commercializing the vaccine. During 1998, we achieved a high level of expression of the MSP-1 protein in the milk of transgenic mice. To express the MSP-1 protein at high quantities, our scientists modified the protein's gene sequence while conserving the overall amino acid sequence of the protein. A U.S. patent has been issued to us for this modification. The MSP-1 protein has been expressed at 2-4 mg/ml in the milk of mice that have incorporated this gene sequence. The MSP-1 protein produced by the mice successfully protected *Aotus nancymai* monkeys in a preclinical vaccine study conducted by and co-authored with the NIAID. This study, titled "A recombinant vaccine expressed in the milk of transgenic mice protects *Aotus* monkeys from a lethal challenge with *Plasmodium falciparum*", was published in the December 18, 2001 *Proceedings of the National Academy of Sciences*. MSP-1 is difficult to express in other recombinant systems, with those other systems producing it in very limited quantities or in forms that may not induce the necessary immune response. The NIAID has funded a contract, managed by Science Applications International Corporation, for the development and production of clinical grade MSP-1 as a malaria vaccine. The scope of work includes developing founder goats that express the MSP-1 antigen in their milk as well as the downstream purification process and final product formulation. A founder animal has the appropriate genetic profile and is the potential start of a herd of transgenic animals capable of producing a desired therapeutic protein. We have developed potential founder animals and we are in the process of evaluating the milking characteristics of these animals. The approved scope of work also includes the submittal of an IND application to the FDA. Our portion of this project has been supported to date with federal funds amounting to at least $6.2 million.

CD137 Antibody

During 2004, we gained access from the Mayo Clinic to the commercial rights for an agonistic antibody to the CD137 receptor in the human immune system, also known as 4-1BB. Agonistic antibodies combine with a receptor or a cell to produce a physiological reaction. In this case, preclinical studies indicate that this antibody stimulates the immune system to recognize and mount a response to solid tumors. If the safety and efficacy of the CD137 antibody is validated in subsequent clinical studies, we anticipate that the required production quantities will be very large. Our transgenic technology platform would be better positioned to economically develop this production capacity than what would be required in a traditional bioreactor based method. We are developing founder animals for this program.

Our collaboration with the Mayo Clinic will provide us with rights to any patents that may be issued under the patent applications that cover the CD137 antibody. Pursuant to the collaboration agreement, we have until April 2006 to exercise an option for an exclusive license to these patents. The Mayo Clinic will provide oversight of the preclinical evaluations. We will produce material that will be tested for bioactivity in human tumor models, and will seek additional grants to develop clinical production and testing, if appropriate, based on the results of the preclinical evaluations. This program is funded under a FLAIR grant awarded by the NCI.

External Program Portfolio

We follow a partnership strategy in our portfolio of external programs, where both our unique intellectual property position and molecular biology expertise are used in the development of a transgenically produced version of the external partner's protein. The advantages to external partners of using our production platform 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. The external portfolio business area also provides us the opportunity for a revenue stream through milestone payments during the development phase and, assuming continuing clinical and development success, subsequent opportunities for long-term product revenues as the external partner's clinical and commercial manufacturing partner. We view this activity as an operating business which currently contributes to the support of our production and regulatory infrastructure and has the potential to provide positive cash flow for investment in our proprietary programs.

The most advanced program in our external portfolio is with Merrimack. The Merrimack program is for MM-093, a recombinant form of human alpha-fetoprotein, or rhAFP. Alpha-fetoprotein is a human blood protein normally produced during pregnancy and, therefore, is not commercially available from fractionation of the human blood supply. MM-093 has been difficult to express in traditional recombinant systems. We have developed goats for Merrimack that express this protein in their milk. In 2002, we agreed to expand this relationship to include production and purification of MM-093. Merrimack completed a Phase I study of MM-093 in 2003 and began Phase II evaluations in 2004, and we continue to deliver purified MM-093 for use in further human clinical studies by Merrimack. Potential indications for MM-093 include autoimmune diseases such as rheumatoid arthritis, multiple sclerosis and myasthenia gravis (a chronic autoimmune neuromuscular disease). Assuming that MM-093 is found to be safe and efficacious in the clinical program, we expect to earn additional revenue totaling several million dollars for production of MM-093 to supply the clinical trials, as well as additional revenues for further production if Merrimack commercializes our transgenically produced version of MM-093. In December 2003, we exercised our option to convert $1.25 million of the receivable owed by Merrimack into Merrimack preferred stock at the same valuation as the other investors in Merrimack's December 2003 financing.

Monoclonal Antibodies (MAbs) and Immunoglobulin (Ig) Fusion Proteins

We believe that our technology platform is well suited to producing difficult-to-express proteins and to establishing large volume production with low capital investment and an assured low cost of goods. Monoclonal antibodies, or MAbs, are proteins generated by an immune system that bind to a specific target. MAbs typically express at reasonable levels in traditional recombinant production systems, but are often required in large quantities due to their applications to chronic disease indications. Immunoglobulin, or Ig fusion proteins, which consist of a MAb fragment linked to a second protein fragment, may be difficult to express due to their complexity.

We are actively participating in the field of MAbs and Ig fusion proteins. We have been granted 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 bioreactor based technologies.

We have two MAb programs with Centocor. In the first, for a transgenically produced form of Remicade®, we have developed founder animals which are being maintained. In the second, for an undisclosed MAb, we have supplied product for preclinical evaluation by Centocor.

We have two MAb programs with Elan Pharmaceuticals, one for Tysabri® (formerly known as Antegren®), which as approved for sale had been manufactured using cell culture produced material before it was withdrawn from the market in March 2005, and another program for an undisclosed antibody. In both programs we have developed founder animals, however both programs were discontinued by Elan in December 2004, and these animals are now being maintained.

Transgenic Technology Platform

Overview

Our technology platform includes the molecular biology expertise and intellectual property to generate transgenic animals, primarily goats and, in some cases, cattle, that express a specific recombinant protein in their milk. We can also perform downstream purification for use in clinical studies. This technology platform is supported by the quality systems and regulatory, clinical development, and information technology infrastructure necessary to bring therapeutic protein products through clinical trials to commercial scale.

The economic and technical advantages of our technology make it 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 capacity expansion 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, as well as some Ig fusion proteins, are examples of recombinant proteins that may not express at economically viable levels in traditional systems.

Our technology platform has been established as an operating infrastructure in goat husbandry, breeding, milking and downstream purification. These operations occur at our biopharmaceutical production facilities in central Massachusetts, where we have approximately 1,400 goats, and at our facilities in Framingham, Massachusetts. Goat husbandry includes veterinary care with a clinic and medicinal supplies, all established within the farm's biosecurity program. The biosecurity program includes barriers to provide separation of the animals from contact with wildlife, separation from people, and quality control monitored feed. Milking is typically performed using modern milking and processing equipment. Clarification to the intermediate bulk material is typically performed using tangential flow filtration equipment that removes much of the fats and casein from the milk. Manufacturing to clinical grade purity under standards of good manufacturing practice occur either in our facilities, the facilities of our partners, or in contracted facilities. During 2002, we established capacity in our Framingham facilities for the purification of recombinant proteins suitable for clinical studies.

We use goats and cattle in our commercial development programs. A goat reaches sexual maturity in about twelve months and gestates in approximately five months. A typical goat will produce an average of approximately 2 liters of milk per day during most of its natural lactation cycle. A cow reaches sexual maturity in about eighteen months and gestates in about nine months. A typical cow will produce an average of approximately 20 liters of milk per day during most of its natural lactation cycle. The species selected for a particular program will depend on a variety of factors, including the expected market size, desired herd size, and anticipated productivity of the desired protein within the animal's mammary gland. In 2002, we obtained broad freedom to operate in cattle technology through a licensing agreement with Pharming Group N.V., which is based in the Netherlands.

We are now using nuclear transfer technology in the development of transgenic animals. The first step in this technology involves the generation of a characterized cell line which has incorporated the specific DNA for expression of the target protein in milk. Individual cells from the cell line(s) are then fused to an animal's ovum after removal of the ovum's own DNA. Thus, the transgenic nucleus of the cell becomes the driver for further development of the embryo, which is then placed in a surrogate female animal. All animals that are born through this process are transgenic. Nuclear transfer may mitigate the impact of long gestation and maturation periods in cattle, by producing a larger number of transgenic animals in one generation. The original methodology we used to develop transgenic animals was called microinjection. In microinjection, the desired DNA was inserted into a fertilized single cell embryo using a needle. Our lead program, ATryn®, used microinjection for generation of the founder animal.

Advantages of Transgenic Technology

We believe that our current and future partners will elect to employ transgenic technology for the production of recombinant proteins in cases where transgenic technology either uniquely enables development of proteins that are hard to express with traditional methods or offers economic and technological advantages over other production systems. These advantages, any one of which may be critical to the decision to proceed with a particular development project, include:

- *Technological Enablement.* Transgenic technology offers the ability to produce certain biotherapeutics that cannot be made in a commercially feasible manner in any other system. Transgenic production systems have the capability to produce therapeutic proteins for large volume indications. In addition, we have achieved consistent expression rates with complex molecules, which may not be producible at commercial scale in cell culture systems. This accomplishment means that transgenics may be a viable production system for some complex proteins regardless of the volume required.

- *Lower Capital Investment.* Developing a herd and providing appropriate production facilities can be accomplished with substantially lower investment than building a cell culture bioreactor facility.

- *Lower Cost of Goods.* Economic factors unique to transgenic production may lower the ultimate cost of goods in most cases. The lower amortization of the initial capital investment, the lower cost of consumable materials and the high productivity of operations result in the cost of transgenically produced products, in most cases, being substantially lower than that of a cell culture derived product.

- *Flexible Production.* Transgenic production offers the ability to match production capacity to the market demand, once the first appropriate animal is identified. If the product's market is larger than originally planned, the incremental investment to breed additional animals and expand capacity is relatively small. In contrast, traditional bioreactor methods are hard assets with a generally fixed capacity. If a bioreactor product's market will support sales significantly higher than the installed capacity can achieve, more bioreactor space needs to be built or acquired at unit costs similar to the original capital investment, with construction times of generally three to five years.

Patents and Proprietary Rights

We currently hold 18 issued or allowed U.S. patents and 111 corresponding foreign patents. Our patents generally expire between 2013 and 2019, with the most significant patents expiring in 2015. Of our patents expiring in 2015, two relate to ATryn®, our lead program. In accordance with ongoing research and development efforts, we have 51 pending U.S. patent applications and 159 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. Limited access has been granted to our technology to Pharming, BioProtein and Nexia Biotechnologies. 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 one covering the production of Prolactin in the milk of transgenic animals.

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 hold licenses to 35 issued U.S. patents and 30 pending U.S. applications. On an international basis, we hold licenses to 63 issued patents and have 102 pending applications. The in-licensed patents that are related to the transgenic platform begin to expire in 2006, beginning with the microinjection patent.

We have exclusive and nonexclusive licenses to specific technologies owned by other parties. We have also concluded an extensive cross-licensing arrangement with Pharming providing broad access to the transgenic cattle platform as well as some additional nuclear transfer technology. Our relationship with Advanced Cell Technologies, Inc., or ACT, focuses on intellectual property concerning cloning and nuclear transfer. Certain of the licenses require us to pay royalties on sales of products which may be derived from or produced using the licensed technology. The licenses generally extend for the life of any applicable patent. We have signed an exclusive, worldwide licensing agreement with ACT that allows us to utilize ACT's patented nuclear transfer technology for the development of therapeutic proteins in the milk of transgenic mammals. ACT has announced that the Board of Patent Appeals and Interferences of the U.S. Patent Office has entered a judgment in an interference proceeding in favor of Geron Corporation on all counts as to the priority of Geron's patents over ACT's U.S. Patent No. 5,945,577, which we license. ACT has also announced that it intends to appeal that decision in a proceeding in U.S. District Court. While this proceeding is pending, we believe that we can continue to rely on the validity of the disputed ACT patent. While we have also licensed nuclear transfer technology from Pharming, we do not know at this time what impact, if any, this proceeding involving ACT may ultimately have on our ability to practice nuclear transfer for the production of animals expressing therapeutic proteins in their milk. Some of our current programs have used this technology. Our lead product, ATryn®, was not developed utilizing this technology.

We rely upon 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 require employees, consultants and certain collaborators to execute confidentiality and invention assignment agreements upon commencement of a relationship with us.

Competition

Many companies, including biotechnology and pharmaceutical companies, are actively engaged in seeking efficient methods of producing proteins for therapeutic or diagnostic applications. Those include companies that are developing transgenic technology using various plant and avian systems, as well as many companies that are building their own cell-culture-based production systems or other traditional protein production methods, and contract manufacturers who are using those systems to produce proteins for others.

Pharming is engaged in the application of transgenic technology in mammals for the production of proteins for therapeutic use in humans. Pharming is primarily engaged in the development of recombinant proteins in the milk of transgenic cows and rabbits and has one product in clinical development that is in Phase III studies. 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 their patents and proprietary rights.

For ATryn®, a number of companies internationally produce and market antithrombin from the fractionation of human plasma. CSL Limited's antithrombin has approximately a 40% share of this market worldwide, but is not approved in the U.S. Bayer is the only company that has commercially available fractionated antithrombin material that is approved for sale in the U.S., which sales represent only about 1% of the worldwide market. Bayer is in the process of selling its plasma products business to NPS Biotherapeutics, Inc. There are a number of providers of plasma-derived antithrombin in Europe, depending on the country. These providers include Octopharma, Grifols, Baxter, Pharmacia, CSL Limited, and LFB.

There are a number of companies worldwide that produce and market human serum albumin from the fractionation of human plasma. We estimate that Bayer and CSL Limited sales represent approximately 30% and 10% market shares, respectively, of the worldwide market for human serum albumin. We are aware of two companies internationally that are developing recombinant forms of human serum albumin derived from yeast cultures. One company, Aventis, is developing its recombinant albumin product for the excipient market. The other lead company is Yoshitomi (formerly Green Cross Corporation) which has been active in developing human albumin through genetic manipulation of Pichia pastorisis (better known as yeast) on a commercial scale for use in Japan and other parts of Asia.

Arriva Pharmaceuticals, Inc. has developed technology for large-scale production of stable non-animal sourced recombinant proteins in *Saccharomyces cerevisiae*, or baker's yeast. Arriva is working with Baxter International to develop a recombinant form of alpha-1 antitrypsin using this technology.

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 U.S. Department of Agriculture and the Environmental Protection Agency. Comparable authorities are involved in other countries, including the EMEA in Europe.

To our knowledge, no therapeutic protein produced in the milk of a transgenic animal has been submitted to the FDA for final regulatory approval or, except for our submission of ATryn® to the EMEA in January 2004, to any other regulatory agency in Europe for final regulatory approval. However, the FDA issued its Points to Consider in August 1995, addressing the Manufacture and Testing of Therapeutic Products for Human Use Derived from Transgenic Animals. Points to Consider, which are not regulations or guidelines, are nonbinding published documents that represent the current thinking of the FDA on a particular topic. Earlier in 1995, comparable guidelines were issued by European regulatory authorities. We believe that our programs satisfactorily address the topics identified in these documents and generally view these publications as positive milestones in the acceptance of the transgenic form of production. Nonetheless, obtaining required regulatory approvals for our transgenically produced products may take several years to complete and is expensive and uncertain.

Regulations in the U.S. setting forth legal requirements for the investigation and commercialization of drug products and medical devices are implemented in accordance with the Food, Drug and Cosmetic Act. Regulations mandating requirements for the development and licensure of biological products are implemented in accordance with the Public Health Service Act, or PHSA. With respect to therapeutic biological products, generally, the standard FDA approval process includes preclinical laboratory and animal testing, submission of an IND to the FDA and completion of appropriate human clinical trials to establish safety and effectiveness. The approval process is comparable in Europe and other countries.

In developing our own transgenic products, we will be required to demonstrate successfully that a given biological product meets PHSA standards, which are, that the product is safe, pure and potent. As a potential manufacturer of biological products developed by others we will also be subject to regulation requiring us to successfully demonstrate that the facility in which a given biological product it is manufactured meets standards designed to ensure that the product continues to be safe, pure and potent. If we do so, then as the manufacturer, we would receive a biological license to market the product in interstate commerce. It is possible, however, that the FDA may not act expeditiously or favorably on requests for approval of a biological license or will require additional data before granting approval. We are required to comply with these regulations to support development and commercialization of products produced in our internal programs and under our contracts with external partners.

Research and Development Costs

During our fiscal years ended January 2, 2005, December 28, 2003 and December 29, 2002, we incurred, $20 million, $18.3 million and $11.9 million, respectively, of development expenses related to internal programs. We also incurred development costs related to our collaborations which are included in cost of revenue. These costs totaled $6.1 million, $11.1

million and $13.1 million in the fiscal years ended January 2, 2005, December 28, 2003 and December 29, 2002, respectively. Of the total spent on research and development, $11.4 million, $8.7 million and $5.1 million, was spent on the ATryn® development program in fiscal years 2004, 2003 and 2002, respectively. 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.

Employees

As of January 2, 2005, we employed 133 people, including 6 part-time and temporary employees. Of our total employees, 89 were engaged in farm operations, clarification processes, quality assurance and control, 13 were engaged in research and development and 31 were engaged in administration, business development and marketing. Of our employees, approximately 12 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. During the third quarter of 2003, we implemented a restructuring plan including a headcount reduction of 13%. Additionally, in February 2004, we announced a further restructuring of our organization to control costs and to support our focus on clinical development and commercialization of our internal pipeline of proprietary products and our portfolio of external programs. In total, these restructurings reduced our headcount from 180 to 127 full time equivalent employees.

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.

ITEM 1A. EXECUTIVE OFFICERS OF THE REGISTRANT

Our executive officers and their respective ages and positions as of March 1, 2005 are as follows:

Name	Age	Position
Geoffrey F. Cox, Ph.D.	61	Chairman of the Board, President and Chief Executive Officer
John B. Green	50	Senior Vice President, Chief Financial Officer and Treasurer
Gregory F. Liposky	50	Senior Vice President, Operations
Harry M. Meade, Ph.D.	58	Senior Vice President, Research and Development
Daniel S. Woloshen	57	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. In 1984, Dr. Cox joined Genzyme Corporation in the UK and, in 1988, became Senior Vice President of Operations in the United States. Subsequently, Dr. Cox was promoted to Executive Vice President for Genzyme, responsible for operations and the pharmaceutical, diagnostic and genetics business units until 1997. Prior to joining Genzyme, Dr. Cox was General Manager of the UK manufacturing operations for Gist-Brocades. Dr. Cox also serves as a Director for Nabi Biopharmaceuticals and serves on the Emerging Companies Section Governing Body of the Biotechnology Industry Organization.

Mr. Green was appointed Senior Vice President in May 2002, having had 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 that, he was Vice President and Assistant Treasurer of TSI Corporation from December 1989 until we acquired TSI in 1994.

Mr. Liposky was appointed Senior Vice President, Operations in May 2002 and was previously Vice President, Operations since January 1999. Prior to that, Mr. Liposky served as Vice President, Contract Manufacturing for Creative Biomolecules, Inc. from 1992 through 1998 and Vice President, Bioprocessing and Operations and Projects Manager for Verax Corporation from 1987 to 1991.

Dr. Meade has been Senior Vice President of Research and Development since 2002. Prior to that time, he was our Vice President of Transgenics Research since August 1994 after serving as Research Director since May 1993. Prior to May 1993, 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., a biotechnology company, where he worked on the technology relating to the production of proteins in milk and was an inventor on the first issued patent covering this process.

Mr. Woloshen was appointed Senior Vice President and General Counsel in May 2002 and was previously Vice President and General Counsel since August 1999. Prior to that, Mr. Woloshen served as Vice President and General Counsel of Philips Medical Systems North America from April 1989 until July 1999.

ITEM 2. PROPERTIES

Our corporate headquarters is located in 12,468 square feet of office space in Framingham, Massachusetts under a lease which expires in June 2006. In 2002, we entered into a Sublease Agreement for an additional 19,888 square feet of office and laboratory space at our existing location in Framingham, Massachusetts, which expires in December 2006. Our research facility is located in approximately 3,900 square feet of laboratory, research and office space leased from Genzyme in Framingham, Massachusetts which automatically renews annually, on a year-to-year basis.

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 1,400 goats. We believe that our owned and leased facilities are adequate for significant further development of commercial transgenic products. We own 135 acres of farm land in eastern New York State which is currently for sale.

ITEM 3. LEGAL PROCEEDINGS

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. The claims arise as a result of our sale of Primedica Corporation to Charles River Laboratories International, Inc. in February 2001, which we believe resulted in the termination of Primedica employees' status as employees of GTC or its affiliates and termination of their options. The plaintiffs contend that the sale of Primedica to Charles River did not constitute a termination of their employment with GTC or its affiliates for purposes of our equity incentive plan and, therefore, that we breached our contractual obligations to them and other Primedica employees who had not exercised their stock options. The complaint demands damages in excess of $5 million, plus interest. We have filed an answer denying all material allegations in the complaint, and are vigorously defending the case and objecting to certification of the claims as a class action. We believe that we have meritorious defenses and that, although the ultimate outcome of the matter cannot be predicted with certainty, the disposition of the matter should not have a material adverse effect on our financial position, results of operations or cash flows.

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

During the fourth quarter of fiscal year 2004, no matter was submitted to a vote of our security holders.

PART II

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

Our Common Stock commenced trading on the NASDAQ National Market System in 1993. The stock's ticker symbol was changed to GTCB on June 3, 2002, in conjunction with changing our name to GTC Biotherapeutics, Inc. Quarterly high and low sales prices for the Common Stock as reported by the NASDAQ National Market are shown below:

	High	Low
2003:		
1st Quarter	$ 1.58	$ 1.01
2nd Quarter	4.34	1.17
3rd Quarter	3.90	2.14
4th Quarter	4.00	2.50
2004:		
1st Quarter	$ 4.47	$ 1.98
2nd Quarter	2.74	1.46
3rd Quarter	2.19	1.52
4th Quarter	1.86	1.27

The records held by the transfer agent indicate that on March 1, 2005 we had approximately 917 shareholders of record.

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

ITEM 6. SELECTED FINANCIAL DATA

The selected financial data set forth below as of January 2, 2005 and December 28, 2003 and for each of the three fiscal years in the period ended January 2, 2005 are derived from our consolidated financial statements included elsewhere in this Report, which have been audited by PricewaterhouseCoopers LLP, independent registered public accounting firm. The selected financial data set forth below as of December 29, 2002, December 30, 2001 and December 31, 2000, and for the years ended December 30, 2001 and December 31, 2000 are derived from audited consolidated financial statements not included in this Report.

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

SELECTED FINANCIAL DATA

(Dollars in thousands except per share data)

	For the Fiscal Years Ended				
	January 2, 2005	December 28, 2003	December 29, 2002	December 30, 2001	December 31, 2000
Statement of Operations Data:					
Revenues:					
Revenue	$ 6,572	$ 9,640	$ 10,379	$ 12,152	$ 12,880
Revenue from joint venture and related party	54	124	—	1,588	3,283
	6,626	9,764	10,379	13,740	16,163
Costs of revenue and operating expenses:					
Cost of revenue	6,107	11,116	13,100	15,075	15,619
Research and development	20,002	18,277	11,869	7,353	3,357
Selling, general and administrative	9,710	10,688	11,319	11,078	9,148
Equity in loss of joint venture	—	—	—	4,078	4,625
	35,819	40,081	36,288	37,584	32,749
Operating loss from continuing operations	(29,193)	(30,317)	(25,909)	(23,844)	(16,586)
Other income and (expenses):					
Interest income	312	1,103	2,028	3,478	3,770
Interest expense	(951)	(508)	(439)	(746)	(1,001)
Realized gain on sale of CRL stock	—	—	—	2,320	—
Other income	339	185	—	—	—
Loss from continuing operations	(29,493)	(29,537)	(24,320)	(18,792)	(13,817)
Discontinued operations					
Income (loss) from discontinued contract research operations, net of taxes	—	—	—	—	(324)
Gain from sale of discontinued contract research operations	—	—	—	2,236	—
Net loss	$ (29,493)	$ (29,537)	$ (24,320)	$ (16,556)	$ (14,141)
Dividends to preferred shareholders			—	—	(74)
Net loss available to common shareholders	$ (29,493)	$ (29,537)	$ (24,320)	$ (16,556)	$ (14,215)
Net loss available to common shareholders per weighted average number of common shares (basic and diluted):					
From continuing operations	$ (0.79)	$ (1.00)	$ (0.86)	$ (0.63)	$ (0.49)
From discontinued contract research operations	—	—	$ —	0.08	(0.01)
Net loss	$ (0.79)	$ (1.00)	$ (0.86)	$ (0.55)	$ (0.50)
Weighted average number of shares outstanding (basic and diluted)	37,360,758	29,562,152	28,353,490	29,975,167	28,373,283

	January 2, 2005	December 28, 2003	December 29, 2002	December 30, 2001	December 31, 2000
Balance Sheet Data:					
Cash, cash equivalents and marketable securities	$ 22,281	$ 31,091	$ 57,349	$ 90,448	$ 66,532
Working capital	10,639	23,967	47,682	74,458	88,389
Total assets	57,301	71,072	95,373	120,443	134,403
Long-term liabilities	9,336	12,582	12,823	80	294
Shareholders' equity	33,653	48,161	68,772	101,950	114,843

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 a leader in the development and production of human therapeutic proteins through transgenic technology. We are focusing our pipeline of internal product programs on recombinant forms of human plasma, or blood proteins currently derived from the human blood supply, for therapeutic purposes. Our lead program, a recombinant form of human antithrombin known as ATryn®, is undergoing review for market authorization in Europe.

We are dependent upon funding from equity financings, partnering programs and proceeds from short and long-term debt to finance operations until such time product sales and royalties occur and we achieve positive cash flow from operations. Our partnering initiatives include licensing and development agreements with collaborative partners for the development, production and purification of transgenically produced forms of therapeutic recombinant proteins. The terms of the agreements typically include non-refundable license fees, funding of research and development, payments based upon the achievement of certain milestones, revenue from sales of product to partners, and royalties on future product sales, if any.

Our key value drivers include the following:

ATryn®

We are seeking regulatory approval of our lead product, a recombinant form of human antithrombin, known as ATryn®, for treatment of patients with hereditary antithrombin deficiency who are undergoing high-risk procedures, such as surgery or childbirth. In January 2004, we submitted a Market Authorization Application, or MAA, to the European Medicines Agency, or EMEA, for approval to market ATryn® in Europe for the hereditary deficiency indication. The application has been accepted for review by the EMEA which will make a determination of the safety and efficacy of ATryn® and assess whether the product is approvable for commercial sale. We have also filed an amended Investigational New Drug application, or IND, with the U.S. Food and Drug Administration, or FDA, to authorize a pivotal clinical study in the HD indication that, together with the data package used in the European submittal, may form the basis for approval of ATryn® in the U.S. We anticipate starting this U.S. trial in the first half of 2005 and that it will last about one year. We believe that ATryn® presents a significant opportunity if it can be expanded into additional indications that result from acquired deficiencies.

rhA

We are developing our recombinant form of human albumin, referred to as rhA, for use as a non-active stabilizer, or excipient, of active biologic ingredients in drug formulations). Our rhA is being developed under the Taurus Joint Venture, in which we currently own a 57% interest and which is consolidated with our results of operations. Fresenius AG owns the remaining interest in the joint venture but has not provided financial support since the formation of the Taurus Joint Venture. During 2004, we initiated the production of qualification batches for rhA for evaluation by potential customers for the excipient, cell culture and *in vitro* fertilization markets. The timetable of development will be dependent upon additional financial resources becoming available to us, or additional marketing or strategic partners providing additional funding.

Malaria Vaccine

We are also developing a therapeutic malaria vaccine that uses as an antigen the difficult-to-express malaria surface protein 1 (MSP-1). We developed potential founder animals in 2004 and production of clinical grade material leading to an IND submittal is anticipated in 2005. Our efforts on this program are funded by NIAID under a contract administered by Science Application International Corporation. Funding from the NIAID represented 15% and 29% of our revenues in 2004 and 2003, respectively.

External Portfolio

We follow a partnership strategy with our portfolio of external programs, whereby both our unique intellectual property position and molecular biology expertise are used to develop transgenic production of an external partner's protein. The external portfolio business area also provides us with the opportunity for a revenue stream through milestone payments during the development phase and, assuming continuing clinical and development success, subsequent opportunities for long-term product revenues as the external partner's commercial manufacturing partner. We view this activity as an operating business which currently contributes to the support of our production and regulatory infrastructure and has the potential to provide positive cash flow for investment in our proprietary programs. The approval of ATryn® may encourage one or more of our external partners to move forward with us in the clinical development of their external programs.

The following table summarizes our revenues from significant external programs in the last three years:

Corporate Partner	For the Fiscal Years Ended January 2, 2005	December 28, 2003	December 29, 2002
Elan (Tysabri® - formerly Antegren®)	27%	—	—
Merrimack	26%	54%	20%
Centocor	20%	1%	—
Elan (undisclosed protein)	—	10%	22%
Bristol Myers-Squibb	—	10%	—
Fresenius[1]	—	—	18%

[1] Before we formed the Taurus Joint Venture in late 2002, the rhA program was funded externally by Fresenius. This table does not include our internal funding of the rhA program after 2002.

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 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 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 based upon the achievement of certain milestones and royalties on future product sales, if any.

We review all contracts at the time of inception to determine the appropriate method of revenue recognition. When there are two or more distinct services or deliverables embedded into one contract, such as development and commercialization or manufacturing services, the contract is considered a multiple element arrangement. For revenue arrangements entered into after July 1, 2003, we account for multiple-element arrangements in accordance with Emerging Issues Task Force (EITF Issue) No. 00-21, or EITF 00-21. For example, we have an agreement that contains multiple deliverables under EITF 00-21. We determined that one delivered item does have standalone value to the customer, but because we could not establish fair value for the undelivered item, we treated the agreement as one unit for accounting purposes. As of the fourth quarter of 2004, we had received approximately $279,000 in cash payments related to the delivered item and had deferred the recognition of revenue under this agreement until the time the undelivered items are delivered.

Revenue is recognized in accordance with EITF 91-6 and SAB 104. 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 and decisions at the partners discretion.

Inventory

We analyze our inventory levels quarterly and estimate our demand for commercial sale and the need to use a portion of the inventory for clinical trials. 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 as well as reviewing for inventory obsolescence and inventory expiration dates. As a result of these estimates and judgments, we recorded approximately $1.1 million of research and development expenses in 2004 reflecting the cost of the inventory that was designated for use in a clinical trial as well as inventory usage for development purposes. During 2003, we recorded a net realizable value write down of approximately $269,000 for our inventory based upon a selling price analysis. A change in any of the estimates which are used for the inventory analysis could have an impact to the financial statements.

Validation Costs

The costs that we have capitalized to date are those costs that are related to FDA or EMEA approval of the manufacturing equipment to be used for the bulk production of ATryn®, which are being depreciated over the expected useful life of the facility. They include the costs of employees and third parties directly involved in the process, direct material consumed in the validation process and incremental fixed overhead. Costs that are excluded from capitalization include maintenance costs, process development/improvement and fixed overhead. As of January 2, 2005 and December 28, 2003, we had approximately $2.9 million and $3.7 million, respectively, of capitalized validation costs, net of accumulated amortization, included in property, plant and equipment. The capitalized validation costs are being depreciated over five years.

Valuation of Intangible and Long Lived Assets

During 2002, upon adopting FAS 142, "Intangible Assets," we performed a cash flow analysis on our intangible marketing rights (see Note 7 to the Notes to Consolidated Financial Statements included in Item 8 of this Report), which resulted in the gross future cash flows being greater than the carrying value of the marketing rights. Judgments used during this analysis included the estimation of the value of revenues to be achieved in the Asian markets which were covered by the marketing rights for both ATryn® and other products produced transgenically. There were no events in 2004 or 2003 that triggered an impairment review.

Results of Operations

The key components to our losses are costs of revenue, research and development expenses, and selling, general and administrative expenses. In September 2003, we implemented an initial restructuring plan followed by a further restructuring in February 2004. As part of these actions, headcount was reduced by approximately 30% and we also renegotiated some of our research agreements with outside contractors. These restructurings resulted in an approximate $6.9 million reduction of expense in 2004 as compared with 2003, including reductions of approximately $2.1 million in cost of revenue, approximately $2.8 million in research and development and approximately $2 million in selling, general and administrative expenses.

Year Ended January 2, 2005 as Compared to Year Ended December 28, 2003

	($ in thousands)			
	January 2, 2005	December 28, 2003	$ Change	% Change
Revenue	$ 6,572	$ 9,640	$ (3,068)	(32)%
Revenue from joint venture and related party	$ 54	$ 124	$ (70)	(56)%
Total Revenue	$ 6,626	$ 9,764	$ (3,138)	(32)%
Cost of revenue	$ 6,107	$ 11,116	$ (5,009)	(45)%
Research and development	$ 20,002	$ 18,277	$ 1,725	9%
Selling, general and administrative	$ 9,710	$ 10,688	$ (978)	(9)%
Interest income	$ 312	$ 1,103	$ (791)	(72)%

Revenue. During 2004, $5.6 million of our revenue was derived from external development programs, primarily the programs with Merrimack Pharmaceuticals, Centocor and Elan Pharmaceuticals, and $1 million of our revenue was derived from the malaria program which is funded by the National Institute of Allergy and Infectious Disease, or NIAID. In December 2004, Elan discontinued the Tysabri® development program and, as result, GTC recognized all of the $1.8 million of revenue associated with the development program. During 2003, $6.9 million of our revenue was derived from external programs, primarily the programs with Merrimack, Elan and Bristol-Myers Squibb, and $2.9 million of our revenue in 2003 was derived from the malaria program. The program with Bristol-Myers Squibb was completed in 2003. The decrease in revenues from external programs reflects the nature and timing of our milestone-based research and development activities for their programs. The decrease in our revenue derived from the malaria program was expected primarily as a result of the timing of activities on the program and revenue from the malaria program is expected to increase in 2005. We expect to continue to see variation in reported revenues on a year-to-year basis.

Cost of revenue and operating expenses. The 2004 expenses included a $944,000 charge associated with the corporate restructuring that was implemented in February 2004, of which approximately $744,000 and $200,000 are included in selling, general and administrative expense and research and development expense, respectively. An additional week of operating expenses is included in 2004 due to the fact that the first quarter was a fourteen week fiscal quarter. The impact of the additional week of operating expense in 2004 was approximately $600,000 as compared with 2003.

Cost of revenue. The decrease in cost of revenue is primarily the result of a decrease in revenue due to the stage of development for external programs for which revenue is being recognized as well as reductions from the restructurings. Included in cost of revenue for 2004 are costs of approximately $1.7 million related to the Elan development program. The level of expenses on our external programs will continue to fluctuate depending upon the stage of development of these individual programs and their progress. The aggregate estimated costs to complete the remaining existing external programs through the development, herd scale up and purification phases is expected to be approximately $1.7 million, with anticipated minimum revenues of $1.9 million excluding success-based milestones. Subsequent to the development phase of the programs, the activities to be performed by us, if any, are to be determined by our partners, who are outside of our control and, therefore, the related costs are unknown.

Research and development expense. The increase in research and development expenses, which is partially offset by the reductions related to the restructuring, relates primarily to support for the regulatory filing for approval to market ATryn® in Europe. The ATryn® related expenses increased to $11.4 million in 2004 as compared with $8.7 million in 2003. Included in the 2004 research and development expenses is $919,000 related to ATryn® inventory designated for use in the upcoming U.S. clinical trial as well as $189,000 of inventory used for development purposes. In 2003, $4.1 million of validation costs were capitalized in connection with the FDA and EMEA approval processes for the manufacturing equipment to be used for the bulk production of ATryn® and are being amortized over five years at a rate of approximately $800,000 per year.

Additionally, in 2004 and 2003, we incurred expenses of $1.7 million and $2.1 million, respectively, in the development of the rhA program, $900,000 and $1.9 million, respectively, in the development of the malaria program and $6 million and $5.6 million, respectively, in other research and development. The decrease in the expenses incurred on the malaria program is primarily a result of the timing of activities on the program. Research and development expenses going forward are expected to fluctuate based on a number of factors including the timing and status of research and development activities for ATryn® and other programs. We cannot estimate the costs to complete these programs due to significant variability in clinical trial costs and regulatory approval processes.

Selling, General and Administrative Expense. The decrease of approximately $978,000 in selling, general and administrative expenses in 2004, reflects lower expenses throughout most areas of selling, general and administrative, primarily as a result of the restructurings, in 2003 and 2004, which included a headcount reduction of approximately 36% in the selling general and administrative area. This was partially offset by approximately $400,000 of costs related to compliance with the Sarbanes-Oxley Act of 2002 and approximately $744,000 of costs associated with the 2004 restructurings. Selling, general and administrative expenses are expected to decrease slightly in 2005 primarily as a result of a decrease in directors and officer's insurance premiums as well as lower costs related to ongoing Sarbanes-Oxley compliance.

Interest income. The decrease in interest income is primarily a result of lower cash and marketable securities balances in 2004 as well as a $155,000 adjustment, resulting in a reduction to interest income, recorded in the first quarter of 2004 related to interest income on our investments during 2003.

Year Ended December 28, 2003 as Compared to Year Ended December 29, 2002

	($ in thousands)			
	December 28, 2003	December 29, 2002	$ Change	% Change
Revenue	$ 9,640	$ 10,379	$ (739)	(7)%
Revenue from joint venture and related party	$ 124	$ —	$ 124	100%
Total Revenue	$ 9,764	$ 10,379	$ (615)	(6)%
Cost of revenue	$ 11,116	$ 13,100	$ (1,984)	(15)%
Research and development	$ 18,277	$ 11,869	$ 6,408	54%
Selling, general and administrative	$ 10,688	$ 11,319	$ (631)	(6)%

Revenue. All of our revenues in 2002, and $6.9 million of our revenues in 2003, were derived from external programs, while $2.9 million of our revenues in 2003 were derived from the malaria program. The reduction in our revenue year to year was primarily due to the inclusion in 2002 of revenue from Fresenius AG in funding the rhA development program prior to the formation of the Taurus Joint Venture. Exclusive of the rhA revenue, for comparison purposes, operating revenues would have increased approximately 14% in 2003.

Cost of revenue and research and development expense. Of the 2003 expenses, approximately $8.7 million was incurred to support the completion of the efficacy study and preparation for regulatory filing for approval to market ATryn® in Europe. This compares with approximately $5.1 million expended in the ATryn® development program in 2002. Additionally, we incurred expenses of $2.1 million in the development of the rhA program and $1.9 million in the development of the malaria program in 2003. We also incurred costs in 2003 on technology improvements and internal product development. During the third quarter of 2003, we implemented a restructuring plan including a headcount reduction of 13%.

Selling, General and Administrative Expense. The decrease of approximately $631,000 in selling, general and administrative expenses in 2003 as compared with 2002 was primarily a result of a reduction of approximately $700,000 in legal expenses in 2003 due to lower external patent costs compared to 2002, which were partially offset by increased expenses related to the acquisition of office and laboratory space of approximately $300,000 for development of our purification capabilities.

Liquidity and Capital Resources

Overview

Our objective is to finance our business appropriately through a mix of equity financings, collaboration and grant revenue, debt financings and interest income earned on our cash and cash equivalents, until such time product sales and royalties occur and we achieve positive cash flow from operations. Our ability to raise future funds will be affected by the progress of clinical trials and the regulatory review of ATryn®, our ability to enter into new or expanded transgenic research and development collaborations, the terms of such collaborations, the results of research and development and preclinical testing of our other internal product candidates, and competitive and technological advances, as well as general market conditions.

We use our cash for a mix of activities focused on enhancing product development and program execution and development and expansion of operational capabilities, which consist primarily of salaries and wages, facility and facility-related costs for office and laboratory space and other outside direct costs. Exclusive of any equity financing in 2005, we anticipate utilizing approximately $25 million of cash in 2005, which includes supporting the launch of ATryn® in Europe and the HD clinical trial in the U.S., as well as anticipated partnering revenues. This cash use also includes approximately $5 million for the manufacture of additional product to supply clinical studies of ATryn® for larger market indications.

We had cash, cash equivalents and marketable securities of $22.3 million at January 2, 2005. We raised an additional $9.7 million in cash, net of offering costs, in January 2005 in a registered direct placement of our Common Stock, which is more fully described under Financing Activities.

We had working capital of $10.6 million at January 2, 2005 compared to $24 million at December 28, 2003.

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 of the fiscal years ended January 2, 2005, December 28, 2003 and December 29, 2002 and have an accumulated deficit of $179.7 million at January 2, 2005. Based on the current rate of cash utilization, management believes that existing cash resources and potential future cash payments from new partnering and licensing programs will be sufficient to fund operations through 2005. The primary sources of additional capital raised in 2002, 2003 and 2004 have been equity and debt financing, and management expects that future sources of funds may include new or expanded partnering arrangements, or the sale of equity or debt-related instruments. However, there can be no assurance that we will be able to raise needed capital on terms that are acceptable to us, or at all. If we are unable to successfully raise additional capital, management has the ability to implement any cost reductions necessary to continue its operations through December 31, 2005

Financing Activities

On August 1, 2003, we issued and sold 3,626,465 shares of our Common Stock at $2.55 per share in a private placement to institutional investors. We also issued to the investors warrants to purchase an aggregate of 906,613 shares of our Common Stock at an exercise price of $3.30 per share. Our proceeds from this sale, net of offering costs, were approximately $8.5 million.

In March 2004, we sold 6,395,298 shares of our Common Stock at $2.35 per share in a registered direct offering to institutional investors. These shares were issued under a shelf registration statement. SG Cowen Securities, as the lead agent, together with Rodman & Renshaw, LLC acted as placement agents for the offering and we paid a placement agent fee for their services. Our proceeds from this sale, net of offering costs of approximately $1.2 million, were approximately $13.9 million.

In January 2005, we sold 7,740,739 shares of our Common Stock at $1.35 per share in a registered direct offering to institutional investors. These shares were issued under a shelf registration. SG Cowen Securities acted as placement agent for the offering and we paid a placement agent fee for its services. Our proceeds from this sale, net of offering costs of approximately $700,000, were approximately $9.7 million.

Credit Facility

Of our $14.2 million of outstanding long-term debt at January 2, 2005, approximately $4.9 million is classified as current. Approximately $9 million was related to a term loan from GE Capital, with monthly payments through 2008, approximately $393,000 was related to capital leases with monthly payments through 2006 and approximately $4.8 million was related to a promissory note payable to Genzyme. The principal is payable in two installments: $2.4 million due on April 4, 2005 and $2.4 million due on April 4, 2006.

In May 2004, we entered into a four year loan agreement with GE Capital in the amount of $10 million, which was used to repay our loan from Silicon Valley Bank. The loan carries a 9.94% interest rate and monthly payments of principal and interest of approximately $253,000. Collateral for the loan includes all of our existing and future acquired assets, excluding intellectual property. This refinancing eliminated a minimum cash covenant that was part of the Silicon Valley Bank loan. Also in connection with the refinancing, we were required to provide $450,000 of cash collateral for our two outstanding stand-by letters of credit, which appears as restricted cash on the balance sheet.

In February 2005, we expanded the term loan with GE Capital to allow us to draw down an additional $2.4 million which we will use to refinance the note payment due to Genzyme in April 2005. The additional amount will be re-paid over three years through March 2008. The loan carries a 10.01% interest rate and is secured by the same collateral as the existing loan with GE Capital.

Cash Flows used in Operating Activities

Cash flows used in operating activities were $20 million, $31.8 million and $23.1 million for fiscal 2004, 2003 and 2002, respectively. Net loss for fiscal year 2004 remained flat while net cash used for operating activities decreased $11.8 million. Cash used in operating activities for 2004 included a net loss of $29.5 million offset by certain non cash charges of approximately $5.7 million, source of funds for increased accrued liabilities of approximately $1.3 million, inventory used for U.S. clinical trials for which the cash costs were incurred in the prior year of approximately $1.1 million, source of funds from a reduction of accounts receivable of approximately $888,000 and an increase in advance payments from customers as a

result of the timing of invoices as well as the deferral of revenue on contracts that contain multiple elements of approximately $410,000.

Cash Flows from Investing Activities

Cash flows from investing activities include $3.4 million in net redemptions of marketable securities in our portfolio and $675,000 in net purchases of capital equipment and further expansion of the transgenic production facility. We anticipate a similar level of capital expenditures company-wide in 2005 as compared to 2004.

Contractual Obligations

The following summarizes our contractual obligations at January 2, 2005, 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	$ 2,276	$ 6,736	$ —	$ —	$ 9,012
Long-term debt obligation – Genzyme	2,386	2,387		—	4,773
Capital lease obligations	203	190	—	—	393
Operating lease obligations	787	704	—	—	1,491
Service agreements for manufacturing	2,648	—	—	—	2,648
Service and sublease agreement with Genzyme	360	—	—	—	360
Total contractual cash obligations	$ 8,660	$ 10,017	$ —	$ —	$ 18,677

We are party to license agreements for certain technologies (see Note 12 to the Notes to Consolidated Financial Statements included in Item 8 of this 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.

We have entered into transactions with related parties (see Note 14 to the Notes to Consolidated Financial Statements included in Item 8 of this Report) in the normal course of business. The terms of these transactions are considered to be at arm's-length.

New Accounting Pronouncements

In March 2004, the Emerging Issues Task Force, or EITF, reached a consensus on Issue No. 03-01, *The Meaning of Other-Than-Temporary Impairment and Its Application to Certain Investments.* EITF Issue No. 03-01 requires the use of fair values calculated in connection with SFAS No. 107, *Disclosures about Fair Value of Financial Instruments*, to be used as the basis for determining whether a cost method investment is impaired. Any impairment would be applied prospectively to all current and future investments, within the scope of EITF Issue No. 03-01, effective in reporting periods beginning after June 15, 2004. EITF Issue No. 03-01 further specifies disclosures an investor should provide about unrealized losses that have not been recognized as other-than-temporary impairments for cost method investments. In September 2004, the Financial Accounting Standards Board, or FASB, issued Staff Position (FSP) EITF Issue No. 03-1-1, which delayed the effective date for the measurement and recognition guidance contained in paragraphs 10-20 of EITF Issue No. 03-01 pending final issuance of FSP EITF Issue 03-1-a. We do not expect the provisions of EITF 03-01 to have a material effect on our results of operations and financial position.

In December 2004, the FASB issued Statement of Financial Accounting Standards No. 123(R) (revised 2004), "Share-Based Payment." Statement 123(R) addresses the accounting for share-based payment transactions in which an enterprise receives employee services in exchange for (a) equity instruments of the enterprise or (b) liabilities that are based on the fair

value of the enterprise's equity instruments or that may be settled by the issuance of such equity instruments. Statement 123(R) requires an entity to recognize the grant-date fair-value of stock options and other equity-based compensation issued to employees in the income statement. Statement 123(R) generally requires that an entity account for those transactions using the fair-value-based method, and eliminates the intrinsic value method of accounting in APB Opinion No. 25, "Accounting for Stock Issued to Employees", which was permitted under Statement 123, as originally issued. Statement 123(R) requires entities to disclose information about the nature of the share-based payment transactions and the effects of those transactions on the financial statements.

Statement 123(R) is effective for public companies that do not file as small business issuers as of the beginning of the first interim or annual reporting period that begins after June 15, 2005 (i.e., our third quarter of 2005). All public companies must use either the modified prospective or the modified retrospective transition method. We expect to use the modified prospective application, without restatement of prior interim periods in the year of adoption. We estimate the impact of this statement to be less than the amounts previously disclosed under SFAS 123.

In November 2004, the FASB issued SFAS No. 151, "Inventory Costs, an amendment of ARB No. 43, Chapter 4," which clarifies the types of costs that should be expensed rather than capitalized as inventory. This statement also clarifies the circumstances under which fixed overhead costs associated with operating facilities involved in inventory processing should be capitalized. The provisions of SFAS No. 151 are effective for fiscal years beginning after June 15, 2005 and we will adopt this standard in our third quarter of fiscal 2005. We have not determined the impact, if any, that this statement will have on our consolidated financial position or results of operations.

On March 31, 2004, the FASB ratified the consensus reached by its EITF on EITF Issue No. 03-06, "Participating Securities and the two-class method under FASB Statement No. 128". EITF Issue No. 03-06 provides additional guidance related to the calculation of earnings per share under FASB Statement No. 128, "Earnings Per Share", which includes application of the two-class method in computing earnings per share, identification of participating securities, and requirements for the allocation of undistributed earnings (and losses) to participating securities. We have reported a net loss and have no securities that share in the net loss and, therefore, the application of EITF Issue No. 03-06 does not require a two-class presentation of earnings per share.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

We have certain financial instruments at January 2, 2005, including a term loan, a promissory note payable and a stand-by letter of credit which are sensitive to changes in interest rates. Our term loan has a carrying value of $9 million which approximates its fair value. Our stand-by letters of credit of $449,360 are required under a facility lease. Our promissory note in the amount of $4.8 million is payable to Genzyme. At January 2, 2005, nothing has been drawn down on the stand-by letters of credit. These instruments are not leveraged and are held for purposes other than trading.

For the term loan and promissory note outstanding, the table below presents the principal cash payments that exist by maturity date.

	($ in 000's)						
	2005	2006	2007	2008	2009	Thereafter	Total
Term Loan	$ 2,276	$ 2,504	$ 2,754	$ 1,478	$ —	$ —	$ 9,012
Promissory Note Payable	2,386	2,387	—	—	—	—	4,773
Total	$ 4,662	$ 4,891	$ 2,754	$ 1,478	$ —	$ —	$ 13,785

The interest rates on the term loan and promissory note payable were 9.94% and 3.51% respectively, at January 2, 2005.

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 borrowings under our promissory note, which interest rate is based on LIBOR plus 1%. We estimate that the hypothetical loss in earnings for one year of borrowings held at January 2, 2005, resulting from a hypothetical 10% increase in interest rates, would not have materially impacted net loss or materially affected the fair value

of rate sensitive instruments. The hypothetical loss was based on financial instruments we held at January 2, 2005 with variable interest rates, fixed rate financial instruments were not evaluated.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTAL SCHEDULES

Financial Statements

Response to this item is submitted as a separate section of this 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.

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 January 2, 2005.

Management's assessment of the effectiveness of our internal control over financial reporting as of January 2, 2005, has been audited by PricewaterhouseCoopers LLP, an independent registered public accounting firm, as stated in their report which is included in this Report at page F-1.

ITEM 9B. OTHER INFORMATION

None.

PART III

ITEM 10. DIRECTORS AND EXECUTIVE OFFICERS OF THE REGISTRANT

The requisite information regarding our directors, executive officers and audit committee members is contained in part under the caption "Executive Officers of the Registrant" in Part I, Item 1A hereof and the remainder is incorporated by reference from the discussion responsive thereto under the captions "Election of Directors" and "Section 16(a) Beneficial Ownership Reporting and Compliance" in our Proxy Statement for the 2005 Annual Meeting of Stockholders to be held on May 25, 2005 (the "2005 Proxy Statement"). 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. This code is available on our website at http://www.gtc-bio.com/investorinfo/corporategovernance.html. A copy of this Code of Business Conduct and Ethics 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 this Code of Business Conduct and Ethics 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

The information set forth under the captions "Compensation and Other Information Concerning Directors and Officers" in the 2005 Proxy Statement is incorporated herein by reference.

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

The information set forth under the captions "Security Ownership of Certain Beneficial Owners and Management" and "Securities Authorized for Issuance Under Equity Compensation Plans" in the 2005 Proxy Statement is incorporated herein by reference.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS

The information set forth under the caption "Transactions with Related Parties" in the 2005 Proxy Statement is incorporated herein by reference. See also Notes 9 and 14 to the Consolidated Financial Statements included in Item 8 of this Report.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

This information set forth under the caption "Auditors" in the 2005 Proxy Statement is incorporated herein by reference.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULE

(a)(1)(2) Financial Statements and Financial Statement Schedule.

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

(3) **Exhibits** As part of this Annual Report on Form 10-K, we hereby file and incorporate by reference the Exhibits listed in the Exhibit Index immediately preceding such Exhibits.

(b) **Exhibits** As part of this Annual Report on Form 10-K, we hereby file the Exhibits listed in the attached Exhibit Index.

(c) **Financial Statement Schedules**

None.

Report of Independent Registered Public Accounting Firm

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

We have completed an integrated audit of GTC Biotherapeutics Inc.'s 2004 consolidated financial statements and of its internal control over financial reporting as of January 2, 2005 and audits of its 2003 and 2002 consolidated financial statements in accordance with the standards of the Public Company Accounting Oversight Board (United States). Our opinions, based on our audits, are presented below.

Consolidated financial statements

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. (the "Company") and its subsidiaries at January 2, 2005 and December 28, 2003, and the results of their operations and their cash flows for each of the three years in the period ended January 2, 2005 in conformity with accounting principles generally accepted in the United States of America. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits. We conducted our audits of these statements in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit of financial statements includes 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. We believe that our audits provide a reasonable basis for our opinion.

Internal control over financial reporting

Also, in our opinion, management's assessment, included in Management's Report on Internal Control Over Financial Reporting appearing under Item 9A, that the Company maintained effective internal control over financial reporting as of January 2, 2005 based on criteria established in Internal Control – Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission ("COSO"), is fairly stated, in all material respects, based on those criteria. Furthermore, in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of January 2, 2005, based on criteria established in Internal Control – Integrated Framework issued by the COSO. The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting. Our responsibility is to express opinions on management's assessment and on the effectiveness of the Company's internal control over financial reporting based on our audit. We conducted our audit of internal control over financial reporting in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. An audit of internal control over financial reporting includes obtaining an understanding of internal control over financial reporting, evaluating management's assessment, testing and evaluating the design and operating effectiveness of internal control, and performing such other procedures as we consider necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinions.

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
March 15, 2005

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

	January 2, 2005*	December 28, 2003
Current assets:		
Cash and cash equivalents	$ 1,835	$ 5,733
Marketable securities	20,446	25,358
Accounts receivable and unbilled contract revenue	725	1,613
Inventory	466	—
Other current assets	1,479	1,592
Total current assets	24,951	34,296
Net property, plant, and equipment	20,279	22,600
Net intangible assets	10,059	11,094
Inventory	—	1,574
Other assets	1,562	1,508
Restricted cash	450	—
Total assets	$ 57,301	$ 71,072
Current liabilities:		
Accounts payable	$ 2,391	$ 2,340
Accrued liabilities	3,517	3,524
Accrued liabilities Genzyme	2,806	1,924
Deferred contract revenue	733	323
Current portion of long-term debt and capital leases	2,479	2,218
Note payable Genzyme	2,386	—
Total current liabilities	14,312	10,329
Long-term debt and capital leases, net of current portion	6,926	7,769
Note payable - Genzyme	2,387	4,773
Deferred lease obligation	23	40
Total liabilities	23,648	22,911
Commitments and contingencies (see Notes 6 and 8)		
Shareholders' equity:		
Preferred stock, $.01 par value; 5,000,000 shares authorized; no shares were issued and outstanding	—	—
Common stock, $.01 par value; 100,000,000 shares authorized; 41,619,974 and 34,749,473 shares issued and 38,799,974 and 31,929,473 shares outstanding at January 2, 2005 and December 28, 2003, respectively	416	347
Additional paid-in capital	222,590	207,535
Treasury stock, at cost, 2,820,000 shares	(9,545)	(9,545)
Accumulated deficit	(179,672)	(150,179)
Accumulated other comprehensive income (loss)	(136)	3
Total shareholders' equity	33,653	48,161
Total liabilities and shareholders' equity	$ 57,301	$ 71,072

* Year ended January 2, 2005 includes 53 weeks while year ended December 28, 2003 includes 52 weeks.

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		
	January 2, 2005*	December 28, 2003	December 29, 2002
Revenues:			
Revenue	$ 6,572	$ 9,640	$ 10,379
Revenue from joint venture and related party	54	124	—
Total revenues	6,626	9,764	10,379
Costs of revenue and operating expenses:			
Cost of revenue	6,107	11,116	13,100
Research and development	20,002	18,277	11,869
Selling, general and administrative	9,710	10,688	11,319
Total cost of revenue and operating expenses	35,819	40,081	36,288
Operating loss	(29,193)	(30,317)	(25,909)
Other income (expense):			
Interest income	312	1,103	2,028
Interest expense	(951)	(508)	(439)
Other income	339	185	—
Net loss	$ (29,493)	$ (29,537)	$ (24,320)
Net loss per common share (basic and diluted)	$ (0.79)	$ (1.00)	$ (0.86)
Weighted average number of common shares outstanding (basic and diluted)	37,360,758	29,562,152	28,353,490
Comprehensive loss:			
Net loss	$ (29,493)	$ (29,537)	$ (24,320)
Other comprehensive loss:			
Unrealized holding loss on available for sale securities	(139)	(181)	(44)
Total other comprehensive loss	(139)	(181)	(44)
Comprehensive loss	$ (29,632)	$ (29,718)	$ (24,364)

* Year ended January 2, 2005 includes 53 weeks while year ended December 28, 2003 includes 52 weeks.

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

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

	Common Stock		Treasury Stock		Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total Shareholders' Equity
	Shares	Amount	Shares	Amount				
Balance, December 30, 2001	30,200	$302	—	—	$197,742	$(96,322)	$228	$101,950
Net loss						(24,320)		(24,320)
Common stock sold under Employee Stock Purchase Plan	337	4			450			454
Common stock issuance to the GTC Savings and Retirement Plan	41				234			234
Proceeds from the exercise of stock options	1				3			3
Acquisition of treasury stock from Genzyme			(2,820)	(9,545)				(9,545)
Stock based compensation					40			40
Unrealized loss on investment							(44)	(44)
Balance, December 29, 2002	30,579	306	(2,820)	(9,545)	198,469	(120,642)	184	68,772
Net loss						(29,537)		(29,537)
Common stock sold under Employee Stock Purchase Plan	382	3			472			475
Common stock issuance to the GTC Savings and Retirement Plan	155	2			170			172
Proceeds from the exercise of stock options	7				10			10
Proceeds from the issuance of common stock, net of offering costs	3,626	36			8,414			8,450
Unrealized loss on investment							(181)	(181)
Balance, December 28, 2003	34,749	347	(2,820)	(9,545)	207,535	(150,179)	3	48,161
Net loss						(29,493)		(29,493)
Common stock sold under Employee Stock Purchase Plan	182	2			347			349
Common stock issuance to the GTC Savings and Retirement Plan	100	1			312			313
Common stock issued under GTC Bonus Plan	111	1			439			440
Proceeds from the exercise of stock options	83	1			118			119
Proceeds from the issuance of common stock, net of offering costs	6,395	64			13,804			13,868
Stock based compensation					35			35
Unrealized loss on investment							(139)	(139)
Balance, January 2, 2005	41,620	$416	(2,820)	$(9,545)	$222,590	$(179,672)	$(136)	$33,653

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		
	January 2, 2005	December 28, 2003	December 29, 2002
Cash flows for operating activities:			
Net loss from operations	$ (29,493)	$ (29,537)	$ (24,320)
Adjustments to reconcile net loss from operations to net cash used in operating activities:			
Depreciation and amortization	4,031	3,476	2,416
Stock based compensation	35	—	40
Amortization of premium (discount) on marketable securities	1,342	(135)	759
Common stock issuance to GTC savings and retirement plan	313	172	234
Inventory write off	—	269	—
Loss on disposal of fixed assets	—	—	140
Recovery of provision for doubtful accounts	—	—	(361)
Changes in assets and liabilities:			
Accounts receivable and unbilled contract revenue	888	566	44
Inventory	1,108	(1,714)	—
Other assets and liabilities	42	(1,081)	(1,452)
Accounts payable	51	(2,108)	2,525
Accrued liabilities—Genzyme Corporation	882	(446)	518
Accrued liabilities	433	(918)	(636)
Deferred contract revenue	410	(315)	(2,982)
Net cash used in operating activities	(19,958)	(31,771)	(23,075)
Cash flows from investing activities:			
Purchase of property, plant and equipment	(1,286)	(3,470)	(6,498)
Sale of property, plant and equipment	611	—	—
Purchase of intangible assets	—	—	(1,517)
Purchase of marketable securities	(13,804)	(24,968)	(52,644)
Redemption of marketable securities	17,235	30,002	85,001
Restricted cash	(450)	—	—
Net cash provided by investing activities	2,306	1,564	24,342
Cash flows from financing activities:			
Proceeds from the issuance of common stock, net of offering costs	13,868	8,450	—
Net proceeds from employee stock purchase plan	349	475	454
Net proceeds from the exercise of stock options	119	10	3
Proceeds from long-term debt	10,386	2,090	10,015
Acquisition of treasury stock from Genzyme	—	—	(4,773)
Repayment of long-term debt	(10,754)	(1,735)	(6,725)
Repayment of principal on capital leases	(214)	(261)	(180)
Net cash provided by (used in) financing activities	13,754	9,029	(1,206)
Net increase (decrease) in cash and cash equivalents	(3,898)	(21,178)	61
Cash and cash equivalents at beginning of the period	5,733	26,911	26,850
Cash and cash equivalents at end of the period	$ 1,835	$ 5,733	$ 26,911
Supplemental disclosure of cash flow information: *			
Cash paid during the period for interest	$ 837	$ 512	$ 423

* See Note 4 for supplemental disclosures of non-cash transactions

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

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

Fiscal years ended January 2, 2005 (fiscal 2004), December 28, 2003 and December 29, 2002 (all tabular $ in thousands, except per share data).

NOTE 1. NATURE OF BUSINESS

We are a leader in the development and production of human therapeutic proteins through transgenic technology. We are focusing our pipeline of internal product programs on recombinant forms of proteins that are derived from human plasma, or blood, for therapeutic uses. Our lead program, a recombinant form of human antithrombin known as ATryn®, is undergoing review for market authorization in Europe. We believe this program is also the first protein produced by transgenic technology to undergo review for market authorization in the U.S. or Europe.

Using our transgenic technology we insert protein-specific DNA into an animal to enable it to produce that specific protein in its milk. We then purify the protein from the milk to obtain the therapeutic product, which is typically administered by injection. We use this technology to focus on those potential therapeutic proteins that are either difficult to express in traditional bioreactor-based technologies, or for those product candidates where the commercial volumes require significant capital investment for production capacity using conventional methods. Human blood proteins that are used for therapeutics may have either or both of these characteristics. In addition to ATryn®, we have two additional recombinant blood proteins in active development in our internal pipeline, recombinant human albumin (rhA) and a recombinant form of alpha-1 antitrypsin (rhAAT).

In addition to our internal programs, we are using our transgenic technology platform in a portfolio of external programs for the development of transgenic production to supply clinical and eventually commercial material for our partners.

We are dependent upon funding from equity financings, partnering programs and proceeds from short and long term debt to finance operations. Our partnering initiatives include licensing and development agreements with collaborative partners for the development, production and purification of transgenically produced forms of therapeutic recombinant proteins. The terms of the agreements typically include non-refundable license fees, funding of research and development, payments based upon the achievement of certain milestones, revenue from sales of product to partners, and royalties on future product sales, if any.

Genzyme Corporation is our largest single shareholder, holding 4,924,919 shares of Common Stock as of January 2, 2005, which represented approximately 13% of our outstanding Common Stock. Genzyme also holds four Common Stock purchase warrants exercisable for 145,000, 288,000, 55,833 and 29,491 shares of our Common Stock at prices of $2.84, $4.88, $6.30 and $6.30 per share, respectively, which were the market prices of the Common Stock at the time the respective Genzyme warrants were issued. The expiration dates of these warrants range from July 2005 through November 2009. All of the shares held by Genzyme (including shares issuable on exercise of Genzyme warrants) are entitled to registration rights.

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 United States Food and Drug Administration (FDA) and other 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 of the fiscal years ended January 2, 2005, December 28, 2003 and December 29, 2002 and have an accumulated deficit of $179.7 million at January 2, 2005. Based on the current rate of cash utilization, management believes that existing cash resources and potential future cash payments from new partnering and licensing programs will be sufficient to fund operations through 2005. The primary sources of additional capital raised in 2002, 2003 and 2004 have been equity and debt financing, and management expects that future sources of funds may include new or expanded partnering arrangements, or the sale of equity or debt-related instruments. However, there can be no assurance that we will be able to raise needed capital on terms that are acceptable to us, or at all. If we are unable to successfully raise additional capital, management has the ability to implement any cost reductions necessary to continue our operations through December 31, 2005.

NOTE 2. SIGNIFICANT ACCOUNTING POLICIES

Basis of Consolidation

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

Our fiscal year ended January 2, 2005, includes 53 weeks.

We consolidate the Taurus hSA LLC joint venture for financial reporting purposes (see Note 13).

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.

Reclassifications

Certain reclassifications have been made to prior years' financial statements to conform to the 2004 presentation.

Cash and Cash Equivalents

Cash equivalents, consisting principally of money market funds and municipal notes purchased with initial maturities of three months or less, are valued at market value.

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 at January 2, 2005 and December 28, 2003 can be summarized as follows:

	January 2, 2005		December 28, 2003	
	Amortized Cost	Estimated Fair Value	Amortized Cost	Estimated Fair Value
Government backed obligations	$ 11,035	$ 10,952	$ 2,073	$ 2,063
Corporate obligations	9,547	9,494	23,127	23,295
Total marketable securities	$ 20,582	$ 20,446	$ 25,200	$ 25,358

Included in marketable securities at January 2, 2005 and December 28, 2003 is $1 million and $8 million, respectively, of auction rate securities classified as available-for-sale securities. Our investment in these securities is recorded at cost, which approximates fair value due to their variable interest rates, which typically reset every 7 to 35 days, and, despite the long-term nature of their stated contractual maturities, we have the ability to quickly liquidate these securities.

At January 2, 2005, December 28, 2003 and December 29, 2002, the change in unrealized gain/loss on marketable securities was $(139,000), $(181,000) and $(44,000), respectively, included in other accumulated comprehensive income and equity. All realized gains/(losses) on available for sale securities in 2004, 2003 and 2002, were immaterial. At January 2, 2005, the contractual maturities of our investments available for sale range from 4 months to 36 months. All of our investments are classified as short-term, which is consistent with their intended use. Unrealized gains / (losses) on marketable securities were approximately $(136,000) and $158,000 at January 2, 2005 and December 28, 2003, respectively.

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 January 2, 2005 and December 28, 2003, approximately 72% and 59%, respectively, of cash, cash equivalents and marketable securities were held by one United States financial institution. Total credit facilities at one commercial bank were $10.6 million at December 28, 2003.

We perform ongoing credit evaluations of our customers' financial conditions and maintain reserves for potential credit losses. There were no write-offs for fiscal 2004, 2003 and 2002.

At January 2, 2005, December 28, 2003 and December 29, 2002, five customers, four customers and two customers, respectively, accounted for 100% of accounts receivable. Five customers accounted for 93% (the largest of which was 27%)

of revenue for the year ended January 2, 2005, four customers accounted for 100% (the largest of which was 54%) of the revenue for the year ended December 28, 2003 and five customers accounted for 81% (the largest of which was 23%) of the revenue for the year ended December 29, 2002.

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 direct costs of the New Zealand goats ("Livestock") are capitalized and amortized using the straight-line method over their estimated useful lives of three years prior to 2003 and five years beginning in 2003.

We capitalize those incremental costs that are incurred in obtaining approval from the FDA or EMEA for manufacturing assets and the related processes for bulk drug production. Under Statement of Financial Accounting Standards (SFAS) No. 34, "Capitalization of Interest Costs," the historical cost of acquiring an asset includes the costs necessarily incurred to bring it to the condition and location necessary for its intended use. The capitalization period begins when expenditures for the asset have been made and activities that are necessary to get the asset ready for its intended use are in progress. Pursuant to regulations of the FDA or the EMEA, a facility and its related manufacturing assets must achieve "process qualification" in order for it to be approved, or "validated," for commercial production. Without approval from the FDA or the EMEA, the facility cannot be placed into service for commercial production; accordingly, the incremental validation costs we incur are an essential part of preparing the related assets for their intended use. Validation by the EMEA will allow us to manufacture products for sale in Europe, which we expect to be the initial market for ATryn®.

The costs that we have capitalized to date are those costs that are related to FDA or EMEA approval of the manufacturing equipment to be used for the bulk production of ATryn® and are being depreciated over the expected life of the facility. These include the costs of employees and third parties directly involved in the process, direct material consumed in the validation process, and incremental fixed overhead. Costs that are excluded from capitalization include costs of maintenance, process development/improvement and fixed overhead. As of January 2, 2005 and December 28, 2003, we had approximately $2.9 million and $3.7 million, respectively, of capitalized validation costs, net of accumulated amortization, included in property, plant and equipment. The capitalized validation costs are being depreciated over five years.

The following is the summary of property, plant and equipment and related accumulated amortization and depreciation as of January 2, 2005 and December 28, 2003.

	Years of Life	January 2, 2005	December 28, 2003
Land	—	$ 1,401	$ 1,401
Buildings	20-30	14,271	14,230
Livestock	3-5	2,842	2,842
Leasehold improvements	lease life	1,764	1,500
Laboratory, manufacturing and office equipment	3-10	11,534	11,167
Laboratory, manufacturing and office equipment—capital lease	3-10	1,960	1,960
		33,772	33,100
Less accumulated amortization and depreciation		(13,493)	(10,500)
Net property, plant and equipment		$ 20,279	$ 22,600

Depreciation and amortization expense was $2,993,000, $2,571,000 and $1,424,000, for the fiscal years ended January 2, 2005, December 28, 2003 and December 29, 2002, respectively. Assets in the amount of $268,000 were disposed of in 2002 with an associated loss of approximately $140,000. Accumulated amortization for equipment under capital lease was $1,400,000, $1,093,000 and $774,000 at January 2, 2005, December 28, 2003 and December 29, 2002, respectively.

In January 2002, we completed a $414,000 purchase of approximately 135 acres of farm land in eastern New York which may be developed as a second production site.

Long-Lived Assets

We review long-lived assets for impairment by comparing the expected cumulative undiscounted cash flows from the assets with their carrying amount. Any write-downs are to be treated as permanent reductions in the carrying amount of the 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 net operating cash flow over the remaining life of the asset.

Accounting for Employee Equity Plans

In December 2002, the Financial Accounting Standards Board (FASB) issued Statement of Financial Accounting Standards No. 148 ("SFAS 148"), Accounting for Stock Based Compensation – Transition and Disclosure. SFAS 148, which was effective for fiscal years ending after December 15, 2002, amended Statement of Financial Accounting Standards No. 123 ("SFAS 123"), Accounting for Stock Based Compensation and provided alternative methods of transition for a voluntary change to the fair value based method of accounting for stock-based compensation. In addition, SFAS 148 amends the disclosure requirements of SFAS 123 regardless of the accounting method used to account for stock-based compensation. We continue to apply APB Opinion 25 and related interpretations in accounting for our employee equity plans. Accordingly, no compensation cost has been recognized for options granted to employees with exercise prices equal to or greater than the fair market value at the grant date. We apply the disclosure only provisions of SFAS 148.

In December 2004, the FASB issued Statement of Financial Accounting Standards No. 123(R) (revised 2004), "Share-Based Payment." Statement 123(R) addresses the accounting for share-based payment transactions in which an enterprise receives employee services in exchange for (a) equity instruments of the enterprise or (b) liabilities that are based on the fair value of the enterprise's equity instruments or that may be settled by the issuance of such equity instruments. Statement 123(R) requires an entity to recognize the grant-date fair-value of stock options and other equity-based compensation issued to employees in the income statement. Statement 123(R) generally requires that an entity account for those transactions using the fair-value-based method, and eliminates the intrinsic value method of accounting in APB Opinion No. 25, "Accounting for Stock Issued to Employees", which was permitted under Statement 123, as originally issued. Statement 123(R) requires entities to disclose information about the nature of the share-based payment transactions and the effects of those transactions on the financial statements.

Statement 123(R) is effective for public companies that do not file as small business issuers as of the beginning of the first interim or annual reporting period that begins after June 15, 2005 (i.e., our third quarter of 2005). All public companies must use either the modified prospective or the modified retrospective transition method. We expect to use the modified prospective application, without restatement of prior interim periods in the year of adoption. Early adoption of this Statement for interim or annual periods for which financial statements or interim reports have not been issued is encouraged. We estimate the impact of this statement to be less than the amounts previously disclosed under SFAS 123. If the compensation cost for our stock-based compensation plans to employees had been determined based on the fair value at the grant dates as calculated in accordance with SFAS 123, our net loss and loss per share for the years ended January 2, 2005, December 28, 2003 and December 29, 2002 would have been increased to the pro forma amounts indicated below:

	January 2, 2005		December 28, 2003		December 29, 2002	
	Net Loss	Net Loss Per Common Share (basic and diluted)	Net Loss	Net Loss Per Common Share (basic and diluted)	Net Loss	Net Loss Per Common Share (basic and diluted)
Net loss reported	$ (29,493)	$ (0.79)	$ (29,537)	$ (1.00)	$ (24,320)	$ (0.86)
Add: *	35	—	—	—	40	—
Deduct: **	(2,253)	(0.06)	(2,417)	(0.08)	(2,854)	(0.10)
Pro Forma net loss	$ (31,711)	$ (0.85)	$ (31,954)	$ (1.08)	$ (27,134)	$ (0.96)

* Total stock-based employee compensation recorded in net loss, as reported.
** Total stock-based employee compensation expense determined under fair value based method for all awards.

The effects of applying SFAS 123 in this pro forma disclosure are not indicative of future amounts. SFAS 123 does not apply to awards prior to 1995, and additional awards in future years are anticipated (see more details in Note 10).

The fair value of each stock option is estimated on the date of grant using the Black-Scholes option-pricing model with the following weighted-average assumption: an expected life of five years, expected volatility of 100% for fiscal 2004 and 2003 and 95% for fiscal 2002, a dividend yield of 0% and a risk-free interest rate of 3.24% for fiscal 2004, 2.96% for fiscal 2003 and 4.47% for fiscal 2002. The average fair value of those options granted during fiscal 2004, 2003 and 2002 was $2.16, $1.22 and $2.53, respectively.

The fair value of the employees' purchase rights was estimated using the Black-Scholes model with the following weighted-average assumptions: a dividend yield of 0%, expected volatility of 100% for fiscal 2004, 98% for fiscal 2003 and 95% for fiscal 2002, an expected life of three months for fiscal 2004, 2003 and 2002 and a risk-free interest rate of 1.24% for 2004, 0.96% for 2003 and 1.61% for 2002. The average fair value of those purchase rights granted during fiscal 2004, 2003 and 2002 was $0.76, $0.70 and $0.95, respectively.

Revenue Recognition and Contract Accounting

We enter into licensing and development agreements with collaborative partners for the development of production and purification of therapeutic recombinant proteins produced in the milk of transgenic animals. The terms of the agreements typically include non-refundable license fees, funding of research and development, payments based upon the achievement of certain milestones and royalties on future product sales, if any.

When there are two or more distinct services or deliverables embedded into one contract, such as development and commercialization or manufacturing services, the contract is considered a multiple element arrangement. For revenue arrangements entered into after July 1, 2003, we account for multiple-element arrangements in accordance with Emerging Issues Task Force (EITF Issue) No. 00-21, or EITF 00-21. When management can determine the fair value of the different elements and the delivered services have value to the customer on a stand-alone basis, then the different elements are accounted for separately. For example, if we enter into an arrangement to perform development services, but we are obligated to perform follow-on manufacturing services, then we must attempt to determine the fair value of both the development services and the manufacturing services. If the terms of both the development and manufacturing services are at fair value, then we will account for the development services separately. If the terms of the development and manufacturing services are not at fair value, but we can determine the fair value of each element, then the total amount of the contract is allocated to each element based on their relative fair values. If we cannot determine the fair value of the development services, but can determine the fair value of the manufacturing services, then revenue will be allocated to the development phase using the residual method. If we cannot determine the fair value of the undelivered services or if the delivered services do not have value to the customer on a stand alone basis, then the contract is accounted for as a single unit of accounting.

Non-refundable license fees, milestones and collaborative research and development revenues under collaborative arrangements, where we are also obligated to provide development services and we can reasonably estimate the effort required to complete our contractual obligations, are recognized as revenue over the period of continuing involvement, using a model similar to the one prescribed by EITF Issue No. 91-6. Under that model, revenue is recognized for non-refundable license fees, milestones and collaborative research and development using the lesser of non-refundable cash received and milestones met or the result achieved using level-of-efforts accounting. Under the level-of-efforts accounting, revenue is based on the cost of effort since the contract's commencement up to the reporting date, divided by the total expected research and development costs from the contract's commencement to the end of the research and development period, multiplied by the total expected contractual payments under the arrangement. Revisions in cost estimates and expected contractual payments as contracts progress have the effect of increasing or decreasing profits in the current period. For development contracts which we cannot reasonably estimate the effort to complete our contractual obligations, revenue is limited to the lesser of costs incurred or non-refundable cash received provided we can reasonably conclude that the costs of completing the contract will not exceed the revenues under the contract. Payments received in advance of being earned are recorded as deferred revenue. Revenue under manufacturing service contracts pursuant to which we are paid for our costs plus a fixed profit margin is recognized as we incur costs. Any up-front payments are spread over the term of the manufacturing arrangement. Revenue under contracts pursuant to which we are paid based on units or volume produced is recognized when title and risk of loss have passed to the customer.

Profits expected to be realized are based on the total contract sales value and our estimates of costs at completion. The sales value is based on achievable milestones and is revised throughout the contract as we demonstrate achievement of milestones. Our estimates of costs include all costs expected to be incurred to fulfill performance obligations of the contracts.

Estimates of total contract costs are reviewed and revised throughout the lives of the contracts, with adjustments to profits resulting from such revisions being recorded on a cumulative basis in the period in which the revisions are made. All revenue recognition estimates are made based upon the current facts and circumstances and are reassessed on at least a quarterly basis. If changes in these estimates or other immaterial adjustments to revenue are identified, the adjustments will be recorded as they become known.

Unbilled contract revenue represents efforts incurred or milestones achieved which had not been billed at the balance sheet date. Deferred contract revenue represents amounts received from customers that exceeded the amount of revenue recognized to date on the balance sheet date.

Inventory

We carry inventory at the lower of cost or market using the first-in, first-out method. We capitalize inventory produced for commercial sale and all of the inventory on hand at January 2, 2005 is related to ATryn® which has not yet been approved for commercial sale. We expect that all of the capitalized inventory will be sold commercially in Europe provided we receive marketing approval. If, at any time, we believe that marketing approval of ATryn® is no longer probable, we will charge the inventory to expense.

During the fourth quarter 2004, we submitted an amendment to our Investigational New Drug (IND) application for the initiation of a clinical study which may be used as a basis for approval of ATryn® in the HD indication in the U.S. We have designated a portion of the ATryn® inventory on hand for use in the clinical trials and accordingly, we recorded a charge in the amount of $919,000, to research and development, reflecting the cost of the inventory. If we should need to use another portion of the capitalized inventory for any additional clinical trials, we would expense the inventory when it was designated for use in such clinical trial.

Also during 2004, we expensed approximately $189,000 to research and development related to usage of inventory for development purposes.

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.

In the fourth quarter of 2003, we recorded a net realizable value write down of inventory of approximately $269,000 which was recorded to cost of revenue as a result of inventoriable costs incurred in excess of the expected net realizable value of the related inventory.

Research and Development Costs

All research and development costs are expensed as incurred. During our fiscal years ended January 2, 2005, December 28, 2003 and December 29, 2002, we incurred, $20 million, $18.3 million and $11.9 million, respectively, of development expense related to internal programs. We also incurred development costs related to our collaborations which are included in cost of revenue. These costs totaled $6.1 million, $11.1 million and $13.1 million in the fiscal years ended January 2, 2005, December 28, 2003 and December 29, 2002, respectively. Of the total spent on research and development, $11.4 million, $8.7 million and $5.1 million, was spent on the ATryn® development program in fiscal years 2004, 2003 and 2002, respectively. These costs include labor, materials and 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), stock to be issued under the defined contribution retirement plan (see Note 10), convertible debt (see Note 8) and convertible preferred stock (see Note 9). We were in a net loss position in 2004, 2003 and 2002, and, therefore, 8.1 million, 6.2 million and 5.6 million of potential common shares, respectively, were not used to compute diluted loss per share, as the effect was antidilutive.

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.

Guarantees

In November 2002, the FASB issued FIN 45, Guarantors Accounting and Disclosure Requirements for Guarantees, Including Indirect Guarantees of Indebtedness of Others, an interpretation of FASB Statements No. 5, 57, and 107 and Rescission of FASB Interpretation No. 34. FIN 45 clarifies the requirements of FASB Statement No. 5, Accounting for Contingencies relating to the guarantors accounting for, and disclosure of, the issuance of certain types of guarantees. For guarantees that fall within the scope of FIN 45, the Interpretation requires that guarantors recognize a liability equal to the fair value of the guarantee upon its issuance. The disclosure provisions of the Interpretation are effective for financial statements of interim or annual periods that end after December 15, 2002. However, the provisions for initial recognition and measurement are effective on a prospective basis for guarantees that are issued or modified after December 31, 2002, irrespective of a guarantor's year-end. The adoption did not effect our results of operations or financial position.

New Accounting Pronouncements

In March 2004, the Emerging Issues Task Force, or EITF, reached a consensus on Issue No. 03-01, *The Meaning of Other-Than-Temporary Impairment and Its Application to Certain Investments.* EITF Issue No. 03-01 requires the use of fair values calculated in connection with SFAS No. 107, *Disclosures about Fair Value of Financial Instruments*, to be used as the basis for determining whether a cost method investment is impaired. Any impairment would be applied prospectively to all current and future investments, within the scope of EITF Issue No. 03-01, effective in reporting periods beginning after June 15, 2004. EITF Issue No. 03-01 further specifies disclosures an investor should provide about unrealized losses that have not been recognized as other-than-temporary impairments for cost method investments. In September 2004, the FASB issued Staff Position (FSP) EITF Issue No. 03-1-1, which delayed the effective date for the measurement and recognition guidance contained in paragraphs 10-20 of EITF 03-01 pending final issuance of FSP EITF Issue No. 03-1-a. We do not expect the provisions of EITF Issue No. 03-01 to have a material effect on our results of operations and financial position.

In December 2004, the FASB issued Statement of Financial Accounting Standards No. 123(R) (revised 2004), "Share-Based Payment", as discussed previously in this Note.

In November 2004, the FASB issued SFAS No. 151, "Inventory Costs, an amendment of ARB No. 43, Chapter 4," ("SFAS 151") which clarifies the types of costs that should be expensed rather than capitalized as inventory. This statement also clarifies the circumstances under which fixed overhead costs associated with operating facilities involved in inventory processing should be capitalized. The provisions of SFAS No. 151 are effective for fiscal years beginning after June 15, 2005 and we will adopt this standard in our third quarter of fiscal 2005. We have not determined the impact, if any, that this statement will have on our consolidated financial position or results of operations.

On March 31, 2004, the FASB ratified the consensus reached by its EITF on EITF Issue No. 03-06, "Participating Securities and the two-class method under FASB Statement No. 128". EITF Issue No 03-06 provides additional guidance related to the calculation of earnings per share under FASB Statement No. 128, "Earnings Per Share", which includes application of the two-class method in computing earnings per share, identification of participating securities, and requirements for the allocation of undistributed earnings (and losses) to participating securities. We have reported a net loss and have no securities that share in the net loss and, therefore, the application of EITF Issue No. 03-06 does not require a two-class presentation of earnings per share.

NOTE 3. SIGNIFICANT AGREEMENTS

Advanced Cell Technologies, Inc. ("ACT")

In June 1999, we signed an exclusive, worldwide licensing agreement with ACT to allow us to utilize ACT's patented nuclear transfer technology for the development of biopharmaceuticals in the milk of transgenic mammals. We believe ACT's proprietary platform technology, when coupled with our transgenic technology, will provide additional patentable approaches to efficiently develop transgenic animals. We paid an upfront license fee of $1,862,000 upon execution of the agreement, which included $1 million of our Common Stock, which is classified as an intangible asset (see Note 7). In addition, we are required to pay royalties to ACT based upon sales by us where ACT's nuclear transfer technology is used. To date, we have paid approximately $223,000 of royalties to ACT.

In January 2005, ACT announced that the Board of Patent Appeals and Interferences of the U.S. Patent Office entered a judgment in an interference proceeding in favor of Geron Corporation against ACT on all counts as to the priority of ACT's U.S. Patent No. 5,945,577, which we license from ACT. ACT has also announced that it intends to appeal that decision in a proceeding in U.S. District Court, during which proceeding we believe that we may continue to rely on the validity of the

disputed patent. While we have also licensed nuclear transfer technology from Pharming, we do not know at this time what impact, if any, this proceeding involving ACT may ultimately have on our ability to practice nuclear transfer for the production of animals expressing therapeutic proteins in their milk. Our lead product, ATryn®, does not utilize this technology.

Pharming Group N.V. ("Pharming")

In June 2002, we obtained licenses to transgenic cattle technology and nuclear transfer technology from Pharming. The license provides 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 which is currently being used in our ongoing activities and, therefore, their associated costs are reported as an intangible asset at January 2, 2005 and are being amortized over a 15-year period, the remaining life of the underlying patents.

Tufts University School of Veterinary Medicine ("Tufts")

We have agreed with Tufts to a non-exclusive licensing agreement to a technique for nuclear transfer technology for which Tufts has rights. Tufts also provides animal husbandry, veterinary care and other services to us, for which we paid Tufts $194,000, $833,000 and $679,000 for the fiscal years ended January 2, 2005, December 28, 2003 and December 29, 2002, respectively. In the fourth quarter of 2003, we significantly reduced our activity with Tufts which resulted in lower payments to Tufts in 2004. Net sales of products derived from transgenic animals produced by Tufts technology, or from their offspring, are subject to royalties payable to Tufts. Our lead product ATryn®, does not utilize the Tufts nuclear transfer technology.

Merrimack Pharmaceuticals, Inc. ("Merrimack")

In June 2003, we executed a definitive agreement with Merrimack for the clinical production and purification of MM-093, a recombinant human alpha-fetoprotein. The terms of the agreement called for deferral of payment of up to $4 million in receivables through the fourth quarter of 2003.

In December 2003, we amended the terms of our agreement with Merrimack for the production and purification of MM-093. Under the revised terms, we converted $1.25 million of the payments owed to us by Merrimack into Merrimack preferred stock. We were paid in cash for amounts owed to us in excess of $1.25 million. We also received an increase in our royalty due from Merrimack on commercial sales of MM-093, if any, as a result of this agreement. This amendment enabled us, as a holder of preferred stock in Merrimack, to participate in a larger portion of the potential value of MM-093. We had approximately $53,000 of billed receivables from Merrimack at January 2, 2005.

Cambrex Bio Science MA, Inc. ("Cambrex")

In August 2002, we entered into a service agreement with Cambrex for Cambrex to provide certain Technology Services relating to biopharmaceutical drug product process transfer, process validation, purification, quality control and quality assurance. As of January 2, 2005, we had paid approximately $4.5 million to Cambrex for services rendered under the contract and we are committed to pay approximately $1.9 million through 2005. The amount paid to Cambrex has either been capitalized as part of our fixed assets, capitalized as part of our inventory (see Note 2), or included in research and development expense.

Malaria Vaccine Contract

The NIAID has funded a contract for the development and production of clinical grade production of MSP-1, as a malaria vaccine. The development work is being performed under the existing NIAID Contract No. NO1-A1-05421 managed by Science Applications International Corporation. The scope of work includes developing founder goats that express the MSP-1 antigen in their milk as well as the downstream purification process and final product formulation. The approved scope of work also includes the submission of an Investigational New Drug application to the FDA. Our portion of this project will be supported completely with federal funds amounting to at least $6.2 million to be paid through September 2007, of which $1.5 million was paid during 2004 and $2.9 million was paid during 2003.

Elan Agreement

During 2004, we contracted with Elan for us to perform development activities related to their Tysabri® (formerly known as Antegren®) product. Non-refundable payments received from Elan through September 30, 2004 were recorded as deferred revenue as we had not agreed on all terms of the arrangement with Elan. Costs incurred in the development program were also deferred and as of September 30, 2004, we had deferred $1.5 million of revenue and $992,000 of costs related to this development program. In December 2004, Elan discontinued the development program and, as result, we recognized all

of the revenue and related costs, including previously deferred costs, associated with the development program. Approximately $1.8 million of revenue and $1.7 million of costs of revenue were recognized in the fourth quarter of 2004. In January 2005, Elan executed a maintenance agreement with us to reduce the herd and to maintain a small number of animals as well as cell lines and cryo-preserved semen relative to the completed program.

NOTE 4. NON-CASH INVESTING AND FINANCING TRANSACTIONS

On April 4, 2002, we bought back 2.82 million shares of our Common Stock directly from Genzyme (see Note 9) which was recorded as treasury stock. We bought the shares for an aggregate consideration of approximately $9.6 million, consisting of approximately $4.8 million in cash and a promissory note to Genzyme for the remaining $4.8 million (see Note 8).

During 2002, we purchased $818,000 of fixed assets and financed these additions with capital lease obligations.

In December 2003, we amended the terms of our agreement with Merrimack for the production and purification of MM-093. Under the revised terms, we converted $1.25 million of payments owed to us by Merrimack into Merrimack preferred stock. We also received an increase in the royalty due from Merrimack on commercial sales of MM-093, if any.

During 2003, we had non cash depreciation related to ATryn® in the amount of $129,000 (see Note 2).

During 2004, we purchased $611,000 of fixed assets and financed these additions with operating lease obligations. Also during 2004, we paid a portion of our employee bonuses in stock amounting to approximately $440,000.

NOTE 5. ACCRUED LIABILITIES

Accrued liabilities included the following:

	At January 2, 2005	At December 28, 2003
Accrued payroll and benefits	$ 1,696	$ 1,714
Accrued bonuses	579	727
Other	1,242	1,083
Total accrued expenses	$ 3,517	$ 3,524

In February 2004, we announced a restructuring of our organization to control costs and to support our focus on clinical development and commercialization of our internal pipeline of proprietary products and our portfolio of external programs. Under the restructuring plan, headcount was reduced by approximately 20% from 159 to 127 full time equivalent employees. In 2003, there were 22 employees terminated during the third quarter as a result of a restructuring. This restructuring included employees from all departments located at both our Framingham and central Massachusetts locations. We recorded severance expense in the amount of $944,000 and $236,000 for the years ended January 2, 2005 and December 28, 2003, respectively. There were no terminations in 2002 and, therefore, we did not record severance expense during 2002. During the years ended January 2, 2005, December 28, 2003 and December 29, 2002, approximately $878,000, $293,000 and $424,000, respectively, had been paid out of the severance reserve. At January 2, 2005, $184,000 remained in accrued liabilities in relation to unpaid severance costs which will be paid out through the third quarter of 2005.

Following is a summary of accrued severance:

Balance at December 30, 2001	$ 659,000
Payments	(484,000)
Balance at December 29, 2002	175,000
2003 restructuring accrual	236,000
2001 restructuring payments	(187,000)
2003 restructuring payments	(106,000)
Balance at December 28, 2003	118,000
2004 restructuring accrual	944,000
2003 restructuring payments	(116,000)
2004 restructuring payments	(762,000)
Balance at January 2, 2005	$ 184,000

NOTE 6. COMMITMENTS AND CONTINGENCIES

We lease equipment and facilities under various operating and capital leases (see Note 8). The deferred lease obligation represents the cumulative difference between actual facility lease payments and lease expense recognized ratably over the lease period. Rent expense for the fiscal years ended January 2, 2005, December 28, 2003 and December 29, 2002 was approximately $1,779,000, $1,893,000 and $1,310,000, respectively.

At January 2, 2005, our future minimum payments required under these leases were as follows:

	Operating	Capital
2005	$ 787	$ 203
2006	450	190
2007	231	—
2008	23	—
2009 and thereafter	—	—
Total	$ 1,491	$ 393
Less amount representing interest		10
Present value of minimum lease payments (see also Note 8)		$ 383

We are a party to license agreements for certain technologies (see Note 3). Certain 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 (see Note 12), we committed to make a minimum annual payment of $360,000 in 2005 which is not included in the above table.

We have entered into manufacturing service agreements for which we are committed to pay approximately $2.6 million through 2005 which is not included in the above table.

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. The claims arise as a result of our sale of Primedica Corporation to Charles River Laboratories International, Inc. in February 2001, which we believe resulted in the termination of Primedica employees' status as employees of GTC or its affiliates and termination of their options. The plaintiffs contend that the sale of Primedica to Charles River did not constitute a termination of their employment with GTC or its affiliates for purposes of our equity incentive plan and, therefore, that we breached our contractual obligations to them and other Primedica employees who had not exercised their stock options. The complaint demands damages in excess of $5 million, plus interest. We have filed an answer denying all material allegations in the complaint, and are vigorously defending the case and objecting to certification of the claims as a class action. We believe that we have meritorious defenses and that, although the ultimate outcome of the matter cannot be predicted with certainty, the disposition of the matter should not have a material adverse effect on our financial position, results of operations or cash flows.

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. The 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. 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.

Intangible assets consist of:

	Amortization Life	January 2, 2005	December 28, 2003
Marketing rights	15 years	$ 11,210	$ 11,210
Accumulated amortization—marketing rights		(3,238)	(2,491)
Net		7,972	8,719
Technology licenses	10 years to 15 years	3,379	3,379
Accumulated amortization — technology licenses		(1,292)	(1,004)
Net		2,087	2,375
Total intangible assets, net		$ 10,059	$ 11,094

Amortization expense was $1,035,000, $1,034,000 and $984,000 in 2004, 2003 and 2002, respectively.

The estimated aggregate amortization expense for the next five years is approximately $1,035,000 per year from 2005 through 2008 and $927,000 for 2009, and $4,994,000 for 2010 and thereafter.

NOTE 8. BORROWINGS

On April 4, 2002, we repurchased 2.82 million shares of our Common Stock from Genzyme, which was recorded as treasury stock. We purchased the shares for an aggregate consideration of approximately $9.6 million, consisting of approximately $4.8 million in cash and a promissory note to Genzyme for the remaining $4.8 million. The $4.8 million promissory note bears interest at the LIBOR plus 1% (LIBOR was at 2.51% at January 2, 2005). The principal is payable in two installments: $2.4 million, due on April 4, 2005 and $2.4 million due on April 4, 2006. The April 4, 2005 payment has been refinanced as discussed below. This note is collateralized by a subordinated lien on all of our assets, except intellectual property.

In March 2002, we entered into a five year Loan and Security Agreement (the "Loan Agreement") with Silicon Valley Bank, or SVB, in the amount of $11.6 million, $5.5 million of which refinanced an existing term loan, and the remainder financed capital additions in 2002 and 2003. In June 2003, we expanded the Loan Agreement by an additional $2,250,000, of which $1.9 million was drawn prior to May 2004. We were required to maintain $18.2 million as unrestricted cash and marketable securities before we would be required to provide cash collateral for the outstanding obligation to SVB, which was approximately $9.6 million at December 28, 2003 Interest on the SVB debt instruments accrued at the prime rate, which was 4% at December 28, 2003.

In May 2004, we entered into a four year loan agreement with General Electric Capital Corporation, or GE Capital, in the amount of $10 million, which was used to repay our outstanding loan from Silicon Valley Bank. The loan carries a 9.94% interest rate and monthly payments of principal and interest of approximately $253,000. Collateral for the loan includes all of our existing and future acquired assets, excluding intellectual property. This refinancing eliminated a minimum cash covenant that was part of the Silicon Valley Bank loan. Also in connection with the refinancing, we were required to provide $450,000 of cash collateral for our two outstanding stand-by letters of credit, which appears as restricted cash on the balance sheet.

In February 2005, we expanded the term loan with GE Capital to allow us to draw down an additional $2.4 million which will be used to refinance the note payment due to Genzyme in April 2005. The additional amount will be re-paid over three years through March 2008. The loan carries a 10.01% interest rate and is secured by the same collateral as the existing loan with GE Capital.

Our long-term debt consisted of the following:

	January 2, 2005	December 28, 2003
GE Capital loan, with monthly payments of $253 through 2008 interest at 9.94%, collateralized all existing and future acquired assets, excluding intellectual property	$ 9,012	$ —
Bank term loan, with monthly payments through March 2008 ($168 in 2004 and $145 in 2003) interest varies as described above, collateralized by real estate	—	9,380
Promissory note to Genzyme, with principal payments of $2,386 in April 2005 and April 2006, interest varies as described above, collateralized by a subordinated lien on all assets except intellectual property	4,773	4,773
Capital lease obligations, with monthly payments of $19 through September 2003 and December 2006, interest at 3.50%, collateralized by property (see also Note 4)	393	607
	14,178	14,760
Less current portion	4,865	2,218
	$ 9,313	$ 12,542

Maturities of long-term debt are as follows:

2005	$ 4,865
2006	5,081
2007	2,754
2008	1,478
2009 and thereafter	—
	$ 14,178

Based on the borrowing rates currently available to us for loans with similar terms and average maturities, the value of the notes payable approximates fair value. Cash paid for interest for the fiscal years ended January 2, 2005, December 28, 2003 and December 29, 2002 was $837,000, $512,000 and $423,000, respectively.

NOTE 9. STOCKHOLDERS' EQUITY

Authorized Shares

Our authorized capital stock consists of 100,000,000 shares of Common Stock, par value $0.01 per share, and 5,000,000 shares of preferred stock, par value $0.01 per share. 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.

Genzyme Stock Buyback

On April 4, 2002, we repurchased 2.82 million shares of our Common Stock from Genzyme, which was recorded as treasury stock. We purchased the shares for an aggregate consideration of approximately $9.6 million, consisting of approximately $4.8 million in cash and a promissory note to Genzyme for the remaining $4.8 million (see Note 8). Our Common Stock was valued at $3.385 per share in this transaction, using the simple average of the high and low transaction prices quoted on the NASDAQ National Market on the previous trading day. Genzyme committed to a 24-month lock-up provision on their remaining 4.92 million shares of our Common Stock, which expired in April 2004.

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 Junior Participating Cumulative Preferred Stock, par value $.01 per share (the "Series C Preferred Stock"), 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.

Common Stock Placements

In August 2003, we issued and sold 3,626,465 shares of our Common Stock at $2.55 per share in a private placement to institutional investors. We also issued warrants to investors to purchase an aggregate of 906,613 shares of our Common Stock at an exercise price of $3.30 per share. We paid SG Cowen a placement agent fee plus warrants to purchase 54,396 shares of our Common Stock on the same terms as the placement warrants. Our proceeds from this sale, net of offering costs of $700,000, were approximately $8.5 million.

In December 2003, we filed a shelf-registration statement (the "Shelf Registration") with the Securities and Exchange Commission which became effective on January 9, 2004. The Shelf Registration allows us to offer and sell from time to time, up to an aggregate of $40 million of Common Stock. The terms and price of any future offerings would be established at the time of the offering.

In March 2004, we sold 6,395,298 shares of our Common Stock at $2.35 per share in a registered direct offering to institutional investors. These shares were issued under a shelf registration statement. SG Cowen Securities, as the lead agent, together with Rodman & Renshaw, LLC acted as placement agents for the offering and we paid a placement agent fee for their services. Our proceeds from this sale, net of offering costs of approximately $1.2 million, were approximately $13.9 million.

In January 2005, we sold 7,740,739 shares of our Common Stock at $1.35 per share in a registered direct offering to institutional investors. These shares were issued under a shelf registration statement. SG Cowen Securities acted as placement agent for the offering and we paid a placement agent fee for its services. Our proceeds from this sale, net of offering costs of approximately $700,000, were approximately $9.7 million.

A summary of our outstanding warrants as of January 2, 2005, of which 1,499,333 are currently exercisable, is as follows:

Common Shares Issuable for	Exercise Price Per Share	Warrant Expiration Date
145,000	$ 2.84	July 3, 2005
20,000	$ 8.75	June 26, 2007
288,000	$ 4.88	December 28, 2008
55,833	$ 6.30	November 12, 2009
29,491	$ 6.30	November 22, 2009
961,009	$ 3.30	August 1, 2008
1,499,333		

As of January 2, 2005, we have reserved 9,025,570 shares of Common Stock, subject to adjustment, for future issuance under the various classes of warrants, the Equity Plans and Employee Stock Purchase Plans.

NOTE 10. EMPLOYEE BENEFIT PLANS

Stock Options and Purchase Plan

In May 1993, the Board of Directors adopted and the shareholders approved the 1993 Equity Incentive Plan (the "Equity Plan"), the 1993 Director Stock Option Plan (the "Director Plan") and the 1993 Employee Stock Purchase Plan (the "Purchase Plan"). In March 2001, the Board of Directors voted to terminate the Director Plan and amend the Equity Plan.

Under the Equity Plan, 2,015,000 shares of Common Stock were issued or reserved for issuance pursuant to incentive stock options, non-statutory stock options, restricted stock awards, stock appreciation rights or stock units in accordance with specific provisions to be established by a committee of the Board of Directors at the time of grant. To date, all options have been issued at 85% or greater of the fair value at the grant date. The Equity Plan also permits us to assume outstanding options in an acquisition without using shares reserved under the Plan. The number of shares reserved for future issuance under the Equity Plan was increased several times over the ensuing years to 5,540,000 at December 30, 2001, which amount includes 200,000 shares transferred from the Director Plan upon its termination.

In May 2002, our shareholders approved the 2002 Equity Incentive Plan (the "2002 Equity Plan"), authorizing a total of 2,500,000 shares for future issuance to our employees, consultants and directors and to our affiliates. The terms of the 2002 Equity Plan are similar to the terms of the Equity Plan.

The 2002 Equity Plan provides (i) that non-employee directors are eligible for grants under the 2002 Equity Plan, (ii) that automatic grants of options to non-employee directors (other than a Chairman of the Board) be made on his or her election or re-election to the Board of Directors, such options to be exercisable for 7,500 shares of each year in the term of office to which such director is elected or re-elected, and having an exercise price equal to the opening price on the date of grant, commencing with the first election or re-election of a non-employee director in 2001 and (iii) that automatic grants of options be made to a non-employee Chairman of the Board on election or re-election to the Board of Directors, such options to be exercisable for 15,000 shares for each year in term of office to which such director is elected or re-elected, and having an exercise price equal to the opening price on the date of grant.

Under both the Equity Plan and the 2002 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.

In May 2004, our shareholders approved the following changes to the 2002 Equity Plan, (i) the Compensation Committee is explicitly authorized to set performance goals to be satisfied before options become exercisable or other awards earned, (ii) the types of awards available under the 2002 Equity Plan were expanded to include restricted stock units, (iii) in addition to the shares under the 2002 Equity Plan all shares that are now or subsequently become available upon termination or forfeited or expired options under the 1993 Equity Plan will be added to the 2002 Equity Plan, (iv) the number of shares authorized for future issuance under the 2002 Equity Plan were increased by 2,000,000 shares, (v) the 2002 Equity Plan as

amended sets forth the annual limits as fixed numbers, namely 400,000 shares for any current participant and 600,000 shares for any new hire, in each case subject to adjustment for changes in GTC's capitalization, (vi) the 2002 Equity Plan as amended clarifies that the exclusion for fair market value consideration includes stock paid in lieu of cash bonuses that would be consistent with past bonus practices and also excludes from the 10% limitation awards that are subject to vesting only if performance criteria are satisfied, (vii) the Board is able to exercise its discretion as to the size, type, and exercisability of awards to non-employee directors, (viii) loans to executive officers and directors for the exercise of options or the purchase of shares will be prohibited, (ix) the repricing of stock options will be prohibited without further stockholder approval, (x) the 2002 Equity Plan will have a term of ten years unless extended by stockholder approval or terminated earlier by the Board, (xi) no options will have a term that can exceed ten years, (xii) 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, change in control, grants to consultants, directors or new hires, awards in lieu of cash compensation and performance vesting.

A summary of the status of our stock option plans as of December 29, 2002, December 28, 2003 and January 2, 2005 and changes during the years ending on those dates is presented below:

	Shares	Weighted Average Exercise Price
Balance at December 30, 2001	2,153,444	$ 8.68
Granted at Fair Value	1,068,320	$ 3.38
Exercised	(750)	$ 4.56
Cancelled	(42,795)	$11.68
Balance at December 29, 2002	3,178,219	$ 6.95
Granted at Fair Value	896,575	$ 1.66
Exercised	(8,020)	$ 1.35
Cancelled	(284,566)	$ 6.47
Balance at December 28, 2003	3,782,208	$ 5.73
Granted at Fair Value	796,100	$ 3.07
Exercised	(83,340)	$ 1.42
Cancelled	(469,170)	$ 6.34
Balance at January 2, 2005, 2003	4,025,798	$ 5.22

At January 2, 2005, December 28, 2003 and December 29, 2002, there were 2,568,700, 2,230,035 and 1,804,885 shares exercisable at a weighted average exercise price of $6.46, $7.16 and $7.91, respectively.

The following table summarizes information about stock options outstanding at January 2, 2005:

Range of Exercise Prices	Number Outstanding	Remaining Contractual Life	Weighted-Average Exercise Price	Number Exercisable	Weighted-Average Exercise Price
$ 0.81 - $1.07	53,500	7.72	$0.89	35,100	$ 0.89
$ 1.11 - $1.45	642,750	8.10	$1.44	265,590	$ 1.44
$ 1.50 - $2.25	443,150	9.34	$2.02	151,810	$ 1.93
$ 2.52 - $3.71	208,330	6.88	$3.28	150,500	$ 3.29
$ 3.80 - $3.80	654,290	7.12	$3.80	392,574	$ 3.80
$ 3.82 - $3.93	4,500	7.08	$3.90	4,000	$ 3.91
$ 3.96 - $3.96	414,400	9.12	$3.96	82,880	$ 3.96
$ 3.97 - $5.03	455,905	5.73	$4.79	399,673	$ 4.77
$ 5.56 - $8.00	544,183	4.83	$7.41	483,793	$ 7.34
$ 8.09 - $37.75	604,790	4.51	$13.43	602,780	$13.44
$ 0.81 - $37.75	4,025,798	6.86	$5.22	2,568,700	$ 6.46

At January 2, 2005, 2,451,328 shares were available for grant.

Under the Purchase Plan, 1,300,000 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. 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. Purchase dates occur every three months for a period of two years from the offering date. Participants may not carry over balances from one purchase date to the next. Offering dates occur every six months.

During 2002, we issued a total of 18,000 options to four outside consultants. The valuation of these options was determined to be $40,000 using the Black-Scholes option pricing model. Since the options were fully vested on the date of grant, the compensation expense of $40,000 for these options was recognized in full during 2002.

In May 2002, our shareholders voted to amend, restate and rename the Purchase Plan as the 2002 Employee Stock Purchase Plan (as amended and restated the "2002 Purchase Plan"). Under the 2002 Purchase Plan, 600,000 additional shares were authorized for future issuance. The amended terms of the 2002 Purchase Plan are substantially similar to the terms of the Purchase Plan. No shares of Common Stock remained available for issuance under the 2002 Purchase Plan as of December 28, 2003. The purchases of Common Stock under the 2002 Purchase Plan during fiscal 2003 totaled 381,429 shares at an aggregate purchase price of approximately $475,000 and during fiscal 2002 totaled 337,392 shares at an aggregate purchase price of approximately $454,000. No compensation expense has been recorded related to the 2002 Purchase Plan. In December 2002, we suspended all new offerings pending the shareholder approval for additional shares in 2003. The ongoing offering from July 1, 2002 continued until there were no shares remaining to cover the purchases.

In May 2003, our shareholders approved the 2003 Employee Stock Purchase Plan (the "2003 Purchase Plan"). Under the 2003 Purchase Plan, 750,000 additional shares were authorized for future issuance. A total of 554,980 shares of Common Stock remained available for issuance under the 2003 Plan as of January 2, 2005. The purchase of Common Stock under the 2003 Purchase Plan during fiscal 2004 totaled 180,584 at an aggregate purchase price of approximately $349,000. Under the 2003 Purchase Plan, the Compensation Committee has established separate six-month offerings every six months, with purchase dates every three months.

In December 2004, the Compensation Committee voted to authorized and approve that the next offering under the 2003 Purchase Plan would commence on January 8, 2005 and terminate on June 24, 2005, with purchase dates for such offering occurring on April 8 and June 24, 2005; and that after June 24, 2005 no further offerings shall be made under such plan until

authorized and approved by further action of the Compensation Committee. Our decision to initiate this change will enable us to continue to apply the disclosure only provision of SFAS 148 for the second quarter 2005 offering.

In February 2004, we recorded compensation expense of $35,000 related to vesting of options for employees which were terminated on February 5, 2004. The Compensation Committee agreed to accelerate vesting of a group of stock options for these employees that were originally scheduled to vest on February 14, 2004. We used the difference between the exercise price and the market value on February 13, 2004 for the accelerated options to calculate the amount of expense.

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 $289,000, $228,000 and $349,000 for the fiscal years ended January 2, 2005, December 28, 2003 and December 29, 2002, respectively.

NOTE 11. INCOME TAXES

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 income tax (benefit) provision from continuing operations consisted of the following:

	Fiscal Years Ended		
	January 2, 2005	December 28, 2003	December 29, 2002
Deferred:			
Federal	$ (10,711)	$ (9,666)	$ (9,177)
State	(1,785)	(1,079)	(1,587)
Foreign	(141)	(81)	—
Change in Valuation Allowance	12,637	10,826	10,764
Total Deferred	$ —	$ —	$ —

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

	Fiscal Years Ended		
	January 2, 2005	December 28, 2003	December 29, 2002
Federal tax—expense (benefit)	(34.0)%	(34.0)%	(34.0)%
State taxes—net	(7.0)	(4.3)	(7.7)
Research and development tax credits	(2.5)	(1.3)	(3.6)
Other	(2.6)	2.9	1.6
Change in valuation allowance	46.1	36.7	43.7
Effective tax rate	0%	0%	0%

The components of the deferred tax assets and liabilities at January 2, 2005 and December 28, 2003, respectively, are as follows (dollars in thousands):

	January 2, 2005	December 28, 2003
Deferred tax assets/(liabilities):		
Net operating loss carryforwards	$ 62,658	$ 60,476
Capitalized research and development expenses	15,772	7,873
Inventory	370	—
Advance payments	295	130
Accrued compensation	298	472
Other accruals	158	194
Tax credits	6,201	4,548
Other	60	—
Depreciation	(705)	(1,239)
Total deferred tax asset	85,107	72,454
Valuation allowance	(85,107)	(72,454)
	$ —	$ —

As of January 2, 2005, we had a federal net operating loss and research and experimentation credit carryforwards of approximately $169 million and $4.2 million, respectively, which may be available to offset future federal income tax liabilities. These carryforwards expire at various dates starting in 2005 and going through 2024. We had approximately $25,000 and $28,000 of federal research and development credits expire in 2004 and 2003, respectively. We also had approximately $813,000 and $11.5 million of federal net operating losses and Massachusetts net operating losses expire in 2004, respectively. As of January 2, 2005, our foreign subsidiaries had NOL carryforwards of $669,000, which do not expire.

We have recorded a deferred tax asset of approximately $4.9 million reflecting the benefit of deductions from the exercise of stock options. This deferred asset has been fully reserved until it is more likely than not that the benefit from the exercise of stock options 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. As required by SFAS No. 109, our management has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets, which are comprised principally of net operating loss and research and experimentation credit carryforwards. Management has determined that it is more likely than not that we will not recognize the benefits of federal and state deferred tax assets and, as a result, a valuation allowance of approximately $85.1 million has been established at January 2, 2005.

Ownership changes, as defined in the Internal Revenue Code, may have limited the amount of net operating loss carryforwards that can be utilized annually to offset future taxable income. Subsequent ownership changes could further affect the limitation in future years.

The American Jobs Creation Act of 2004 (the "Act") was signed into law on October 22, 2004. The Act contains numerous amendments and additions to the U.S. corporate income tax rules. None of these changes, either individually or in the aggregate, are expected to have any significant effect on our income tax liability.

NOTE 12. ARRANGEMENTS WITH GENZYME CORPORATION

From our inception, certain facilities and support services, including both research and administrative support, have been provided by Genzyme. For these services, we were charged $2,919,077, $3,514,851 and $3,338,598 for the fiscal years ended January 2, 2005, December 28, 2003 and December 29, 2002, respectively. These charges, which are set by Genzyme,

represent an allocation of our proportionate share of Genzyme's overhead costs using formulae which our management believes are reasonable based upon our use of the facilities and services. Also included in this amount are other costs for all periods presented, including payroll costs that are directly attributable to us and have been paid by Genzyme and charged to us.

Equity Position

Genzyme is our largest single shareholder, holding 4,924,919 shares of Common Stock as of January 2, 2005, which represented approximately 13% of the outstanding Common Stock. Genzyme also holds four Common Stock purchase warrants exercisable for 145,000, 288,000, 55,833 and 29,491 shares of our Common Stock at prices of $2.84, $4.88, $6.30 and $6.30 per share, respectively, which were the market prices of our Common Stock at the time the respective Genzyme warrants were issued. The expiration dates of these warrants range from July 2005 through November 2009. All of the shares held by Genzyme (including shares issuable on exercise of Genzyme warrants) are entitled to registration rights. Genzyme owned approximately 14% of our Common Stock on a fully diluted basis. Subsequent to the January 2005 registered direct offering, Genzyme owns approximately 11% of our outstanding Common Stock and approximately 12% on a fully diluted basis.

On April 4, 2002, we bought back 2.82 million shares of our Common Stock from Genzyme which was recorded as treasury stock (see Note 9). The $4.8 million promissory note bears interest at the LIBOR plus 1% (LIBOR was at 2.51% at January 2, 2005). The principal is payable in two installments: $2.4 million, due on April 4, 2005 and $2.4 million due on April 4, 2006. This note is collateralized by a subordinated lien on all of our assets, except intellectual property.

In April 1993, we entered into several agreements under which Genzyme has agreed to provide us various services, facilities and funding. Those still in effect are described below:

Services Agreement

Under the Services Agreement, we received certain basic laboratory and administrative support services in exchange for a fixed monthly fee. The monthly fee was adjusted annually based on the services to be provided and changes in Genzyme's cost of providing the services. If we requested additional services from Genzyme, we agreed to pay Genzyme fully allocated costs of those services. Under the Services Agreement, we made payments of $101,000 and $1,012,000 for the fiscal years ended December 28, 2003 and December 29, 2002, respectively. We no longer receive services from Genzyme under this agreement.

Sublease Agreement

Under the Sublease Agreement, we leased certain laboratory, research and office space from Genzyme in exchange for fixed monthly rent payments which approximate the estimated current rental value for such space. In addition, we reimburse Genzyme for it's pro rata share of each appropriate facilities' operating costs such as maintenance, cleaning, utilities and real estate taxes. The sublease is automatically renewed each year and renewals are subject to early termination of the sublease by either party after the initial five-year term. Under the Sublease Agreement, we made payments for the fiscal years ended January 2, 2005, December 28, 2003 and December 29, 2002, of $352,000, $356,000 and $281,000, respectively, and is committed to make a minimum annual rental payment of approximately $360,000 in 2005.

Technology Transfer Agreement

Under the Technology Transfer Agreement dated May 1, 1993, Genzyme transferred to us substantially all of its transgenic assets and liabilities, assigned its relevant contracts and licensed to us technology owned or controlled by it and relating to the production of recombinant proteins in the milk of transgenic animals (the "Field") and the purification of proteins produced in that manner. The license is worldwide and royalty free as to Genzyme, although we are obligated to Genzyme's licensors for any royalties due to it. As long as Genzyme owns less than 50% of GTC, Genzyme may use the transferred technology, or any other technology it subsequently acquires relating to the Field, for internal purposes only without any royalty obligation to us.

Research and Development Agreement

On July 31, 2001, we entered in to a services agreement with Genzyme pursuant to which Genzyme may perform manufacturing, research and development and regulatory services for the ATryn® program. Our payments to Genzyme are on a cost plus 5% basis. Related costs of $2,390,000, $2,934,000 and $2,090,000 were incurred in 2004, 2003 and 2002, respectively. These costs included amounts for clinical and regulatory support provided to us by Genzyme BV for the filing of the MAA for submission to market ATryn® in Europe. This agreement is operating on a month to month basis through August 31, 2005.

In June of 2003, we entered into a Services Agreement with Genzyme under which we provide certain services to Genzyme for which Genzyme shall pay a monthly amount to us based on a rate we agreed upon with Genzyme, through December 31, 2004.

First Negotiation Right for Commercializing ATryn®

If we choose to commercialize ATryn® with a marketing partner outside of Asia, Genzyme has an exclusive first right of negotiation for exclusive commercialization rights. This right is triggered on an indication-by-indication basis at such time as we apply for marketing approval with a regulatory authority. This right does not apply if we have already entered into a collaboration or other agreement with a prospective research, development and marketing partner prior to such regulatory submission. It also no longer applies to the hereditary deficiency indication which has been filed with the EMEA.

ATIII LLC Re-Acquisition

In 1997, we established the ATIII LLC joint venture with Genzyme for the marketing and distribution rights of ATryn® in all territories other than Asia. In July 2001, we reacquired Genzyme's ownership interest in the 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.

NOTE 13. JOINT VENTURES

Taurus hSA LLC

In late 2002, we restructured our relationship with Fresenius AG for the therapeutic blood expander market into a joint venture, called Taurus hSA LLC or the Taurus Joint Venture, to include the development of rhA program as an excipient. The Taurus Joint Venture will manage development of our rhA for both the excipient and blood expander markets. We currently have a 57% interest in the joint venture. Each party has the right, but not the obligation, to make future contributions to the Taurus Joint Venture. The joint venture structure allows the development of the excipient market with the potential to attract additional marketing or strategic partners that may also assist with the financing of the joint venture. Ownership interests will be adjusted based on future levels of financial participation from existing and new partners. We are engaged in ongoing discussions with third parties to obtain further financing for the Taurus Joint Venture and we have also developed alternative plans to advance the joint venture using its existing resources with limited external financing. Along with Fresenius, we have made available all relevant commercial licenses, manufacturing and marketing rights, and intellectual property to enable the joint venture to operate worldwide in both the excipient and blood expander markets. The existence of the Taurus Joint Venture is perpetual unless terminated or dissolved earlier in accordance with the terms of the agreement. Upon any liquidation, sale or other disposition of all, or substantially all of the assets of the Taurus Joint Venture, and after the payment of debts and liabilities, expenses of liquidation and any reserves for unforeseen liabilities or in-kind distributions, the net proceeds would be applied and distributed first to Fresenius and then to us, each according to relative percentage interest. Each member would also have reversion rights to any intellectual property it contributes to the Taurus Joint Venture. We consolidate the Taurus Joint Venture on our financial statements for financial reporting purposes.

NOTE 14. OTHER RELATED PARTY TRANSACTIONS

Board of Directors

All Directors who are not also our employees receive an annual retainer of $12,000, payable quarterly. Members of the Audit Committee also receive an annual retainer of $4,000, payable quarterly and members of the Compensation Committee also receive an annual retainer of $2,000, payable quarterly. The Chairman of the Audit Committee receives an additional annual retainer of $6,000, payable quarterly and the Chairman of the Compensation Committee receives an additional annual retainer of $3,000, payable quarterly. Members of the Board receive a per meeting fee of $1,000 and an additional $1,000 per standing committee meeting that is not in conjunction with the Board meeting. These fees are reduced to $500 for participation via conference call.

NOTE 15. 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	Japan	Europe	Total
2004	$ 6,379	$ 3	$ 244	$ 6,626
2003	9,759	5	—	9,764
2002	8,447	6	1,926	10,379

Of our long-lived assets, $8 million of intangible assets are located in an offshore subsidiary and the remaining $2 million are located in the United States.

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

	United States	United Kingdom	New Zealand	Total
2004	$ 17,534	$ 4,140	$ 617	$ 22,291
2003	$ 19,250	$ 5,638	$ 794	$ 25,682

NOTE 16. UNAUDITED RESULTS OF QUARTERLY OPERATIONS

	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
2004				
Revenue	$ 1,066	$ 1,439	$ 924	$ 3,197[1]
Operating loss	(8,643)	(6,098)	(7,013)	(7,439)
Net loss	(8,576)	(6,259)	(7,150)	(7,508)[2]
Net loss per share — basic and diluted	(0.26)	(0.16)	(0.18)	(0.19)

	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
2003				
Revenue	$ 1,744	$ 4,111	$ 2,164	$ 1,745
Operating loss	(7,549)	(6,090)	(7,902)	(8,776)
Net loss	(7,393)	(6,008)	(7,606)	(8,530)[3]
Net loss per share — basic and diluted	(0.27)	(0.21)	(0.25)	(0.27)

(1) In the fourth quarter of 2004, the development program with Elan was discontinued and therefore all of the previously deferred revenue was recognized in the fourth quarter of 2004.

(2) In the fourth quarter of 2004, we recorded a charge of approximately $919,000 to research and development, reflecting the cost of inventory that was designated for use in a clinical study. Also in the fourth quarter of 2004, we recognized previously deferred contract costs of approximately $992,000 as a result of the discontinuation of the Elan development program.

(3) In the fourth quarter of 2003, we recorded a net realizable value write down of approximately $269,000 for our ATryn® inventory based upon an analysis of the then current selling price of plasma-based antithrombin. Also in the fourth quarter of 2003, we had an increase in research and development expenses related to the regulatory and clinical expense required for the preparation of the January 2004 submission of our MAA to the EMEA for ATryn®.

NOTE 17. SUBSEQUENT EVENTS

In January 2005, we sold 7,740,739 shares of our Common Stock at $1.35 per share in a registered direct offering to institutional investors. These shares were issued under a shelf registration (see Note 9). SG Cowen Securities acted as placement agent for the offering and we paid a placement agent fee for its services. Our proceeds from this sale, net of offering costs of approximately $700,000, were approximately $9.7 million.

In February 2005, we expanded the term loan with GE Capital to allow us to draw down an additional $2.4 million which will be used to refinance the note payment due to Genzyme in April 2005. The additional amount will be re-paid over three years through March 2008. The loan carries a 10.01% interest rate and is secured by the same collateral as the existing loan with GE Capital.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities and 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 15th day of March 2005.

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)	March 15, 2005
/s/ John B. Green John B. Green	Chief Financial and Accounting Officer (Principal Financial and Accounting Officer)	March 15, 2005
/s/ Robert W. Baldridge Robert W. Baldridge	Director	March 15, 2005
/s/ Kenneth A. Bauer Kenneth A. Bauer	Director	March 15, 2005
/s/ Francis J. Bullock Francis J. Bullock	Director	March 15, 2005
/s/ James A. Geraghty James A. Geraghty	Director	March 15, 2005
/s/ Michael J. Landine Michael J. Landine	Director	March 15, 2005
/s/ Pamela W. McNamara Pamela W. McNamara	Director	March 15, 2005
/s/ Marvin L. Miller Marvin L. Miller	Director	March 15, 2005
/s/ Alan W. Tuck Alan W. Tuck	Director	March 15, 2005

EXHIBIT INDEX
to Form 10-K for the Year Ended January 2, 2005

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 filed with the Secretary of the Commonwealth of Massachusetts on October 3, 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) and incorporated by reference herein.
3.1.3	Articles of Amendment to the Restated Articles of Organization 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) 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 filed with the Commission on June 2, 2000 (File No. 333-38490) 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 filed on June 1, 2001 (File No. 0-21794) 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 filed on June 3, 2002 (File No. 0-21794) and incorporated by reference herein.
3.2	By-Laws of GTC, as amended. Filed as Exhibit 3.1 to GTC's Form 10-Q for the quarter ended July 4, 1999 (File No. 0-21794) 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) (the "GTC S-1") and incorporated by reference herein.
4.2	Warrant to Purchase Common Stock, dated July 3, 1995, issued to Genzyme Corporation ("Genzyme"). Filed as Exhibit 10.5 to GTC's Quarterly Report on Form 10-Q for the period ended July 2, 1995 (File No. 0-21794) and incorporated by reference herein.
4.3	Warrant to Purchase Common Stock, dated as of June 26, 1997, issued to Government Land Bank d/b/a The MassDevelopment. Filed as Exhibit 4 to GTC's Quarterly Report on Form 10-Q for the period ended June 29, 1997 (File No. 0-21794) and incorporated by reference herein.
4.4	Warrant to Purchase Common Stock, dated as of December 28, 1998, issued to Genzyme. Filed as Exhibit 4.11 to GTC's Annual Report on Form 10-K for the year ended January 3, 1999 (File No. 0-21794) and incorporated herein by reference.
4.5	Warrant to Purchase Common Stock, dated November 12, 1999, issued to Genzyme. Filed as Exhibit 8 to Genzyme's Amendment No. 6 to Schedule 13D (File No. 005-46637) filed with the Commission on November 24, 1999 and incorporated by reference herein.
4.6	Warrant to Purchase Common Stock, dated November 12, 1999, issued to Genzyme. Filed as Exhibit 9 to Genzyme's Amendment No. 6 to Schedule 13D (File No. 005-46637) filed with the Commission on November 24, 1999 and incorporated by reference herein.
4.7	Form of Common Stock Purchase Warrant. Filed as Exhibit 10.2 to GTC's Current Report on Form 8-K filed on August 4, 2003 (File No. 0-21794) and incorporated by reference herein.
4.8	Registration Rights Agreement between GTC and certain Stockholders named therein. 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) and incorporated by reference herein.
4.9	Shareholder Rights Agreement, dated as of May 31, 2001, 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 filed on June 1, 2001 (File No. 0-21794) and incorporated by reference herein.

4.10 Registration Rights Agreement, dated as of July 30, 2003, between GTC and the Purchasers named therein. Filed as Exhibit 10.3 to GTC's Current Report on Form 8-K filed on August 4, 2003 (File No. 0-21794) and incorporated by reference herein.

10.1* Agreement between GTC and Gene Pharming Europe B.V., dated as of September 21, 1994. Filed as Exhibit 10.49 to GTC's Form S-1 and incorporated by reference herein.

10.2 Research and Development Agreement between GTC and Genzyme, dated as of May 1, 1993. Filed as Exhibit 10.1 to the GTC S-1 and incorporated by reference herein.

10.3 Sublease Agreement between GTC and Genzyme, dated as of May 1, 1993. Filed as Exhibit 10.3 to the GTC S-1 and incorporated by reference herein.

10.4 License Agreement between GTC and Genzyme, as successor to IG Laboratories, Inc., dated as of May 1, 1993. Filed as Exhibit 10.4 to the GTC S-1 and incorporated by reference herein.

10.5.1* Cooperation and Licensing Agreement between GTC and Tufts University, dated September 6, 1988, as amended through May 13, 1993 (the "Cooperation and Licensing Agreement"). Filed as Exhibit 10.18 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.

10.5.2 Amendment No. 7, dated April 1, 1993, to Cooperation and Licensing Agreement. Filed as Exhibit 10.6 to GTC's Quarterly Report on Form 10-Q for the period ended October 1, 1995 (File No. 0-21794) (the "GTC October 1995 10-Q") and incorporated by reference herein.

10.5.3 Amendment No. 8, dated October 21, 1993, to Cooperation and Licensing Agreement. Filed as Exhibit 10.7 to the GTC October 1995 10-Q and incorporated by reference herein.

10.5.4* Amendment No. 9, dated December 1, 1993, to Cooperation and Licensing Agreement. Filed as Exhibit 10.8 to the GTC October 1995 10-Q and incorporated by reference herein.

10.5.5 Amendment No. 10, dated November 1, 1993, to Cooperation and Licensing Agreement. Filed as Exhibit 10.9 to the GTC October 1995 10-Q and incorporated by reference herein.

10.5.6 Amendment No. 11, dated May 25, 1995, to Cooperation and Licensing Agreement. Filed as Exhibit 10.10 to the GTC October 1995 10-Q and incorporated by reference herein.

10.5.7* Amendment No. 14, effective as of September 6, 1997, to Cooperation and Licensing Agreement. Filed as Exhibit 10.6.7 to GTC's Annual Report on Form 10-K for the year ended December 29, 2002 (File No. 0-21794) (the "GTC 2002 10-K") and incorporated by reference herein.

10.5.8* Amendment No. 16, effective as of September 6, 2000, to Cooperation and Licensing Agreement. Filed as Exhibit 10.6.8 to the GTC 2002 10-K and incorporated by reference herein.

10.5.9* Amendment No. 18, effective as of September 6, 2001, to Cooperation and Licensing Agreement. Filed as Exhibit 10.6.9 to the GTC 2002 10-K and incorporated by reference herein.

10.6* United States Patent No. 4,873,191 Sublicense Agreement between Xenogen Corporation (formerly DNX, Inc.) and Genzyme Regarding Transgenic Experimental Animals and Transgenic Mammary Production Systems, dated February 1, 1990; and letter of amendment, dated April 19, 1991. Filed together as Exhibit 10.3 to GTC's Amended Quarterly Report on Form 10-Q for the period ended June 29, 2003 (File No. 0-21794) (the "GTC 2003 June 10-Q/A") and incorporated by reference herein.

10.7 Lease dated March 26, 1999 between GTC and NDNE 9/90 Corporate Center LLC. Filed as Exhibit 10.1 to the GTC July 1999 10-Q and incorporated by reference herein.

10.8 Hazardous Materials Indemnity Agreement, December 28, 1998, between the GTC and Genzyme. Filed as Exhibit 10.28.5 to GTC's Annual Report on Form 10-K for the year ended January 2, 2000.

10.9* 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 period ended June 30, 2002 (File No. 0-21794) filed on August 2, 2002 (the "GTC June 2002 10-Q") and incorporated by reference herein.

10.10* 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 the GTC June 2002 10-Q and incorporated by reference herein.

10.11* Exclusive Development and License Agreement, dated as of June 8, 1999, between GTC and Advanced Cell Technology, Inc. Filed as Exhibit 10.21 to GTC's Annual Report on Form 10-K for the year ended December 30, 2001 (File No. 0-21794) and incorporated by reference herein.

10.12.1* Purchase Agreement between GTC and Genzyme, 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) (the "GTC September 2001 10-Q") and incorporated by reference herein.

10.12.2* Services Agreement between GTC and Genzyme, dated as of July 31, 2001. Filed as Exhibit 10.3 to the GTC September 2001 10-Q and incorporated by reference herein.

10.12.3 Collaboration Agreement among GTC, Genzyme Corporation, and ATIII LLC dated as of January 1, 1998. Filed as Exhibit 10.2 to GTC's quarterly Report on Form 10-Q/A filed on November 26, 2003 and incorporated by reference herein.

10.12.4 Amended and Restated Collaboration Agreement among GTC, Genzyme and ATIII LLC, dated as of July 31, 2001. Filed as Exhibit 10.4 to the GTC September 2001 10-Q and incorporated by reference herein.

10.13 Letter Agreement by and between GTC and Genzyme, dated as of April 4, 2002. Filed as Exhibit 10.4 to GTC's Quarterly Report on Form 10-Q for the period ended March 31, 2002 (File No. 0-21794) filed on May 1, 2002 (the "GTC March 2002 10-Q") and incorporated by reference herein.

10.14 Subordinated Secured Promissory Note in the amount of $4,772,850 executed by GTC and made to Genzyme, dated as of April 4, 2002. Filed as Exhibit 10.5 to the GTC March 2002 10-Q and incorporated by reference herein.

10.15* Sublease Agreement by and between GTC and Antigenics, Inc., dated July 16, 2002. Filed as Exhibit 10.4 to the GTC June 2002 10-Q and incorporated by reference herein.

10.16* Limited Liability Company Agreement of Taurus hSA LLC dated as of December 20, 2002. Filed as Exhibit 10.20.1 to GTC's 2002 10-K and incorporated by reference herein.

10.17* Contribution and License Agreement by and between GTC and Taurus hSA LLC dated as of December 20, 2002. Filed as Exhibit 10.20.2 to GTC's 2002 10-K and incorporated by reference herein.

10.18* Service Agreement by and between GTC and Cambrex Bio Science MA, Inc., dated as of August 20, 2002. Filed as Exhibit 10.21 to GTC's 2002 10-K and incorporated by reference herein.

10.19.1* Agreement Relating to the Production of Clarified Goat Milk Containing Recombinant Human Alpha Fetoprotein by and between GTC and Merrimack Pharmaceuticals, Inc., dated as of June 27, 2003 (the "Merrimack Agreement"). Filed as Exhibit 10 to GTC's 2003 June Form 10-Q/A and incorporated by reference herein.

10.19.2 First Amendment, dated as of December 11, 2003, to the Merrimack Agreement. Filed as Exhibit 10.21.2 to the GTC 2003 10-K and incorporated by reference herein.

10.20.1** 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) and incorporated by reference herein.

10.20.2** GTC 2002 Equity Incentive Plan. Filed as Exhibit 10.6 to GTC's Amended Quarterly Report on Form 10-Q for the period ended March 31, 2002 (File No. 0-21794) and incorporated by reference herein.

10.21** GTC 2002 Employee Stock Purchase Plan. Filed as Exhibit 10.7 to the GTC March 2002 10-Q and incorporated by reference herein.

10.22 GTC Form of Confidential and Proprietary Information Agreement signed by GTC employees. Filed as Exhibit 10.9 to the GTC S-1 and incorporated by reference herein.

10.23 GTC Form of Agreement Not to Compete. Filed as Exhibit 10.10 to the GTC S-1 and incorporated by reference herein.

10.24 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.

10.25** Employment Agreement, dated as of March 27, 1996, between GTC and Harry Meade. Filed as Exhibit 10.44 to GTC's Quarterly Report on Form 10-Q for the period ended March 31, 1996 and incorporated by reference herein.

10.26.1** Amended and Restated Employment Agreement, dated as of August 28, 1997, between GTC and John B. Green. Filed as Exhibit 10.2 to the GTC September 1997 10-Q and incorporated by reference herein.

10.26.2** Amendment No. 1 to Employment Agreement between GTC and John B. Green. Filed as Exhibit 10.3 to GTC's Quarterly Report for the period ended September 27, 1998 (File No. 0-21794) and incorporated by reference herein.

10.27** Executive Employment Agreement, dated as of July 18, 2001, between GTC and Geoffrey F. Cox. Filed as Exhibit 10.2 to the GTC September 2001 10-Q and incorporated by reference herein.

10.28** Executive Employment Agreement, dated as of February 9, 2002 between GTC and Paul K. Horan. Filed as Exhibit 10.30 to GTC's 2002 10-K and incorporated by reference herein.

10.29** Management Agreement between GTC and Daniel Woloshen dated as of May 27, 1999. Filed as Exhibit 10.1 to GTC's Quarterly Report on Form 10-Q for the period ended March 30, 2003 (File No. 0-21794) (the "GTC March 2003 10-Q") and incorporated by reference herein.

10.30** Management Agreement between GTC and Gregory Liposky dated as of June 14, 2000. Filed as Exhibit 10.2 to the GTC March 2003 10-Q and incorporated by reference herein.

10.31 Master Security Agreement between General Electric Capital Corporation and GTC, dated as of May 26, 2004. Filed as Exhibit 99.1 to GTC's Form 8-K filed on May 27, 2004 and incorporated by reference herein.

10.32 Promissory Note made by GTC in favor of General Electric Capital Corporation, dated May 26, 2004. Filed as Exhibit 99.2 to GTC's Form 8-K filed on May 27, 2004 and incorporated by reference herein.

10.33** Executive Compensation Disclosure Schedule. Filed herewith.

10.34 Promissory Note, dated February 25, 2005, by and between General Electric Capital Corporation and GTC. Filed as Exhibit 10.1 to GTC's Form 8-K filed on March 2, 2005 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.

99 Important Factors Regarding Forward-Looking Statements. Filed herewith.

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* 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.

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

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

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

Pamela W. McNamara
Chief Executive Officer
CRF, Inc.
Former CEO, Arthur D. Little

Marvin L. Miller
Executive Chairman
Onconova Therapeutics, Inc.
Former President and CEO
Nextran, an affiliate of
Baxter Healthcare Corporation

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.

Gregory F. Liposky
Senior Vice President Operations
GTC Biotherapeutics, Inc.

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

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.

INDEPENDENT ACCOUNTANTS

PricewaterhouseCoopers LLP
Boston, MA

EXTERNAL LEGAL COUNSEL

Palmer & Dodge LLP
Boston, MA

MARKET FOR COMMON STOCK

Nasdaq National Market System
Trading Symbol: GTCB

REPORT ON FORM 10-K

GTC's Annual Report on Form 10-K for the year ended January 2, 2005 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, or by calling (508) 620-9700 x5374.

ANNUAL MEETING

The Annual Meeting of Shareholders will be held on Wednesday, May 25, 2005 at 2:00 p.m. at the Forefront Center for Meetings and Conferences, 404 Wyman Street, Waltham, Massachusetts 02451.

Design: Schenkel/Stegman Communications Design, www.schenkelstegman.com Executive Photography: Patrick O'Connor Photography

GTC BIOTHERAPEUTICS, INC.
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