

PE  
12-31-02

Annual Report Texas  
Biotechnology  
Corporation

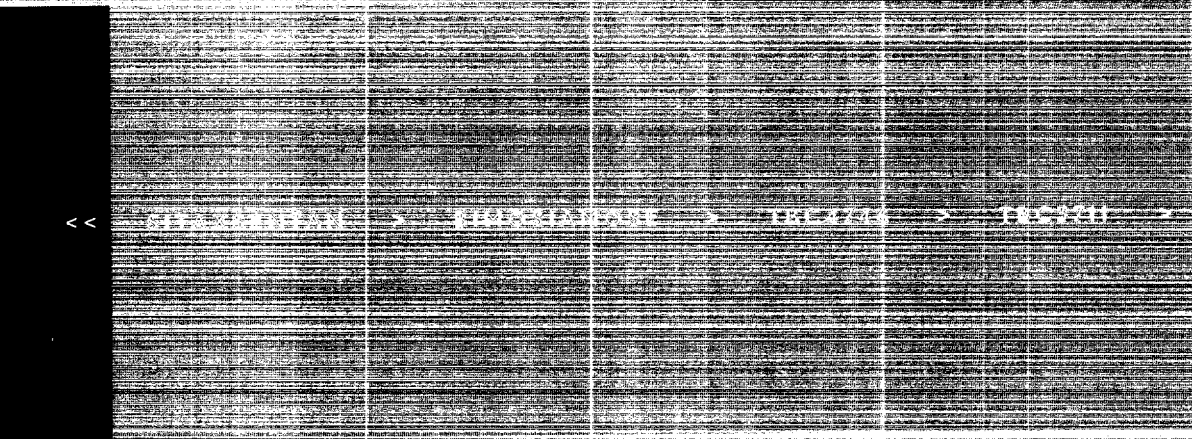


RECD S.E.C.  
APR 14 2003  
1086

FOCUSING ON THE DEVELOPMENT OF OUR MOST PROMISING NEW THERAPIES >>

PROCESSED  
T APR 15 2003  
THOMSON  
FINANCIAL

A handwritten signature in the bottom right corner of the page.



ENCYSIVE™  
K E M A S I C S

## DEAR SHAREHOLDERS

There are five core reasons why we are excited about the future. First, we have demonstrated the ability to develop novel compounds that work. Argatroban and sitaxsentan are proven examples. Second, we have successfully navigated the FDA, garnering an FDA approval for Argatroban, a drug that is now being marketed by our partner GlaxoSmithKline (GSK). Third, we have an outstanding clinical development team that has successfully brought sitaxsentan into pivotal Phase III clinical trials. Fourth, on the heels of sitaxsentan is a promising product pipeline that includes three high quality compounds in early stages of development, two of which are being developed by partners. And finally, our research team is addressing two key target groups that we believe will cement our franchise in the cardiovascular and inflammatory disease markets.

We will be seeking shareholder approval to change our name. We have chosen one that we believe better represents how we want to be perceived as we move toward becoming a commercial leader in cardiovascular and inflammatory disease therapeutics. I'll discuss this in more detail a bit later in this letter.

**A NEW FOCUS - IMPACT ON CLINICAL DEVELOPMENT** In the past, research and clinical development served as the Company's foundations. However, success in the clinic alone does not ensure a path to profitability. In January, we implemented a restructuring of the company to focus our resources on only those efforts that will lead to the commercial success of this organization. As a result, our clinical development team is now entirely focused on the development of sitaxsentan, a compound designed to treat pulmonary arterial hypertension (PAH). We believe sitaxsentan to be our flagship compound. With the potential of serving a market of 100,000 patients worldwide, it holds great promise in generating significant revenue for Texas Biotechnology. Additionally, by obtaining full rights to the compound from ICOS in 2003, we will capture greater shareholder value if sitaxsentan continues to stay on course to reach the marketplace.

We have made substantial progress in the clinical development of sitaxsentan this year. We successfully completed STRIDE I (Sitaxsentan To Relieve Impaired Exercise in PAH) and will be reporting data from the trial at the American Thoracic Society annual meeting in mid-May. After meeting with the FDA in December 2002, we are finalizing the protocol for our pivotal STRIDE II trial and plan to begin enrollment in the second quarter of 2003.

To maintain focus on sitaxsentan, we have turned over all further clinical development of Argatroban to GlaxoSmithKline. GSK was our partner in developing Argatroban and has full responsibility for the sales and marketing of the compound. Through our royalty agreement with GSK, Argatroban generated \$3.5 million in revenue for our company last year. Argatroban is a testament to the strength of our research, clinical development, and regulatory teams. Of course, as our "first born," Argatroban holds a special place in our company's history and we are proud to monitor its continued growth in the market. However, by relinquishing its further development to GSK, we conserve the cash and resources required to move sitaxsentan forward to FDA approval.

We have three promising compounds that are in the early stages of development. TBC3711 is our next generation endothelin-A receptor antagonist that has performed well in Phase I clinicals. It will be placed back into the hands of our development team once sitaxsentan has completed Phase III clinical trials. Two different partners are taking our other compounds through clinical development. Bimosiamose is in Phase II trials for asthma and psoriasis with our majority owned affiliate Revotar Biopharmaceuticals AG. We will be reporting data from these trials in the first and second halves of 2003. TBC4746, a VLA-4 inhibitor for asthma, is in development with our partner Schering-Plough Corporation. In June 2002, Schering's selection of this orally available small molecule triggered a milestone payment. We are optimistic about a successful completion of its final preclinical testing and initiation of Phase I clinical trials.



FRONT ROW (LEFT TO RIGHT)

**Bruce D. Given, M.D.** President and CEO  
**Richard A.F. Dixon, Ph.D.** Senior Vice President, Research and CSO

BACK ROW (LEFT TO RIGHT)

**Tommy A. Brock, Ph.D.** Vice President, Pharmacology & Preclinical Development  
**Heather Giles, Ph.D.** Vice President, Strategic Planning  
**Stephen L. Mueller, CPA** Vice President, Finance & Administration, Secretary and Treasurer  
**Philip M. Brown, M.D., J.D.** Vice President, Clinical Development  
**Daniel J. Thompson, MA, DABT** Director, Regulatory Affairs  
**Patrick Ward, R.Ph., MBA** Executive Director, Business Development  
**Pamela Mabry, PHR** Director, Human Resources

**Texas Biotechnology Corporation**  
 6700 West Loop South, Suite 400  
 Bellaire, Texas 77401  
[www.tbc.com](http://www.tbc.com)

**BOARD OF DIRECTORS**

**John M. Pietruski**  
 Chairman Of The Board  
 Retired Chairman and  
 Chief Executive Officer  
 Sterling Drug Inc.

**Bruce D. Given, M.D.**  
 President and  
 Chief Executive Officer  
 Texas Biotechnology Corporation

**Ron J. Anderson, M.D.**  
 President and  
 Chief Executive Officer  
 Parkland Health and  
 Hospital System

**Frank C. Carlucci**  
 Chairman Emeritus  
 The Carlyle Group

**Robert J. Cruikshank**  
 Retired Senior Partner  
 Deloitte & Touche LLP

**Richard A.F. Dixon, Ph.D.**  
 Senior Vice President, Research  
 Chief Scientific Officer  
 Texas Biotechnology Corporation

**Suzanne Oparil, M.D.**  
 Director Vascular Biology and  
 Hypertension Program  
 The University of Alabama  
 at Birmingham

**William R. Ringo, Jr.**  
 Retired President of Oncology  
 and Critical Care  
 Eli Lilly and Company

**James A. Thomson, Ph.D.**  
 President and  
 Chief Executive Officer  
 RAND Corporation

**James T. Willerson, M.D.**  
 President  
 The University of Texas –  
 Houston Health Science Center

**OFFICERS**

**Bruce D. Given, M.D.**  
 President and  
 Chief Executive Officer

**Richard A.F. Dixon, Ph.D.**  
 Senior Vice President, Research  
 Chief Scientific Officer

**Stephen L. Mueller**  
 Vice President, Finance and  
 Administration  
 Secretary and Treasurer

**ANNUAL MEETING**

The Annual Meeting of the  
 Stockholders will be held at  
 9:00 a.m., Friday, May 16, 2003  
 InterContinental Houston Hotel  
 2222 West Loop South  
 Houston, Texas 77027

**CORPORATE HEADQUARTERS**

6700 West Loop South, Suite 400  
 Bellaire, Texas 77401  
 Telephone: (713) 796-8822  
 Facsimile: (713) 796-8232  
 Internet: [www.tbc.com](http://www.tbc.com)

**AUDITORS**

KPMG LLP  
 Houston, Texas

**CORPORATE COUNSEL**

Porter & Hedges, L.L.P.  
 Houston, Texas

**INTELLECTUAL PROPERTY COUNSEL**

Wood, Phillips, Katz,  
 Clark & Mortimer  
 Chicago, Illinois

**COMMON STOCK INFORMATION**

Texas Biotechnology Corporation  
 Common Stock trades on the  
 Nasdaq National Market under  
 the symbol "TXBI." The Company  
 has not declared any dividends  
 and does not expect to pay any  
 common stock dividends in the  
 foreseeable future.

**TRANSFER AGENT AND REGISTRAR**

The Bank of New York  
 (800) 524-4458  
 E-mail address:  
[shareowner-svcs@stockbny.com](mailto:shareowner-svcs@stockbny.com)  
 Web site: [www.stockbny.com](http://www.stockbny.com)

Address shareholder inquiries to:  
 Shareholder Relations  
 Department  
 P.O. Box 1158  
 Church Street Station  
 New York, New York 10286

Send certificates for transfer and  
 address changes to:  
 Receive and Deliver Department  
 P.O. Box 11002  
 Church Street Station  
 New York, New York 10286

**INVESTOR RELATIONS**

Ann Tanabe  
 Telephone: (713) 796-8822  
 Fax: (713) 796-8232  
 Web site: [www.tbc.com](http://www.tbc.com)

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

Form 10-K

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

For the fiscal year ended December 31, 2002

or

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

Commission file number: 0-20117

**Texas Biotechnology Corporation**

(Exact name of Registrant as specified in its charter)

Delaware  
(State of Incorporation)

13-3532643  
(I.R.S. Employer  
Identification Number)

7000 Fannin, 20th Floor  
Houston, Texas 77030  
(713) 796-8822

(Address and telephone number of principal executive offices and zip code)

Securities registered pursuant to Section 12(b) of the Act:  
None

Securities registered pursuant to Section 12(g) of the Act:  
Common Stock, \$.005 per share  
Title of Class  
Preferred Stock Purchase Rights  
Title of 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 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes  No

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

Indicate by check mark whether the registrant is an accelerated filer (as defined in Rule 12b-2 of the Act). Yes  No

The approximate aggregate market value of voting stock held by nonaffiliates of the registrant is \$169,054,000 as of June 28, 2002.

The number of shares outstanding of each of the registrant's classes of common stock as of March 12, 2003:

Title of Class	Number of Shares
Common Stock, \$.005 par value	43,916,898

Documents incorporated by reference:

Document	Form 10-K Parts
Definitive Proxy Statement, to be filed within 120 days of December 31, 2002 (specified portions)	III

[THIS PAGE INTENTIONALLY LEFT BLANK]

## CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Form 10-K contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. All statements other than statements of historical fact included in and incorporated by reference into this Form 10-K are forward-looking statements. These forward-looking statements include, without limitation, statements regarding our estimate of the sufficiency of our existing capital resources and our ability to raise additional capital to fund cash requirements for future operations, and regarding the uncertainties involved in the drug development process and the timing of regulatory approvals required to market these drugs. Although we believe that the expectations reflected in these forward-looking statements are reasonable, we cannot give any assurance that such expectations reflected in these forward-looking statements will prove to have been correct.

When used in this Form 10-K, the words "expect," "anticipate," "intend," "plan," "believe," "seek," "estimate" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Because these forward-looking statements involve risks and uncertainties, actual results could differ materially from those expressed or implied by these forward-looking statements for a number of important reasons, including those discussed under "Management's Discussion and Analysis of Financial Condition and Results of Operations", "Additional Risk Factors" and elsewhere in this Form 10-K.

You should read these statements carefully because they discuss our expectations about our future performance, contain projections of our future operating results or our future financial condition, or state other "forward-looking" information. You should be aware that the occurrence of any of the events described in the risk factors and elsewhere in this Form 10-K could substantially harm our business, results of operations and financial condition and that upon the occurrence of any of these events, the trading price of our common stock could decline, and you could lose all or part of your investment.

We cannot guarantee any future results, levels of activity, performance or achievements. Except as required by law, we undertake no obligation to update any of the forward-looking statements in this Form 10-K after the date of this Form 10-K.

This Form 10-K may contain trademarks and service marks of other companies.

## PART I

### ITEM 1 — BUSINESS

#### Overview

Texas Biotechnology Corporation was incorporated in Delaware in 1989 and is sometimes referred to in this report as TBC, we or us. We are a biopharmaceutical company focused on the discovery, development and commercialization of novel, synthetic, small molecule compounds for the treatment of a variety of cardiovascular, vascular and related inflammatory diseases. Our research and development programs are focused on inhibitors (also referred to as antagonists or blockers) that can interrupt certain disease processes. Our programs seek to address unmet medical needs in areas where our compounds will have the greatest likelihood of improving the lives of patients suffering from cardiovascular diseases, thrombocytopenia, pulmonary arterial hypertension ("PAH"), heart failure and inflammatory diseases such as asthma.

Argatroban is our first marketed product. Argatroban was approved by the U.S. Food and Drug Administration ("FDA") in 2000 for the prophylaxis or treatment of thrombosis in patients with heparin-induced thrombocytopenia ("HIT") and for patients with or at risk for HIT undergoing percutaneous coronary intervention ("PCI"). Argatroban was approved in Canada in 2002 for use as anticoagulant therapy in patients with heparin-induced thrombocytopenia syndrome ("HITS"). The drug is being marketed in the U.S. and Canada by GlaxoSmithKline, plc ("GSK") and has been on the market in the U.S. and Canada since November 2000 and June 2002, respectively. GSK is our development, manufacturing and marketing partner for Argatroban.

Presently, we have four major product development programs.

- *Endothelin Antagonist Program.* We are developing sitaxsentan, an endothelin (A) receptor antagonist, or ET<sub>A</sub>, for the treatment of PAH. During June 2000, we formed a partnership, ("ICOS-TBC"), with ICOS Corporation ("ICOS") to develop and commercialize ET<sub>A</sub> receptor antagonists. During 2002, ICOS-TBC successfully completed a Phase IIb/III clinical trial in PAH with sitaxsentan. TBC3711, a second generation ET<sub>A</sub>, has previously completed Phase I clinical trials and may be developed for cardiovascular or other diseases. In January 2003, ICOS announced that they had reached a conclusion that joint development of the endothelin receptor antagonist program by ICOS-TBC should not continue. ICOS and TBC are currently negotiating the terms pursuant to which TBC could independently continue the program. The financial terms of this transaction are subject to ongoing negotiations between the two companies.
- *Thrombosis.* During 2002, we completed a Phase II human clinical trial for Argatroban as a mono-therapy treatment for acute ischemic stroke. The clinical trial met the primary endpoint based on safety. In light of a lack of a positive overall efficacy trend and the high risk and high costs associated with stroke trials, it is unlikely that we will proceed independently with a full Phase III program. Currently, Argatroban is being evaluated, in a clinical trial, in combination with recombinant tissue Plasminogen Activator ("rt-PA") as a new approach to the treatment of acute ischemic stroke by an investigator at the University of Texas Medical School at Houston.
- *Vascular Inflammation Program.* Revotar Biopharmaceuticals AG ("Revotar"), our majority owned German affiliate located in Berlin is developing a selectin antagonist, bimosiamose, for the treatment of asthma and psoriasis. The intravenous form of the drug demonstrated positive anti-inflammatory effects in Phase II clinical trials. Revotar was formed during 2000, to further the development of this program. Revotar has completed Phase I clinical trials for asthma utilizing an inhaled form of bimosiamose. A Phase IIa clinical trial is currently being conducted with an inhaled form of bimosiamose and a Phase IIa clinical trial in psoriasis is planned to commence during 2003, using a topical formulation. A Phase IIa proof-of-concept clinical trial in psoriasis, completed during 2002 with an injectable form of bimosiamose, demonstrated signs of activity. We are also conducting research with respect to other cell adhesion molecules including vascular cell adhesion molecule, or VCAM, junctional adhesion molecules, or JAM 2/3 and several integrins including very late antigen 4, or VLA-4,  $\alpha 4\beta 7$  and others to develop antagonists for the treatment of asthma, rheumatoid arthritis, multiple sclerosis, restenosis and inflammatory bowel disease. We have signed a collaboration and license agreement for the VLA-4 program with Schering-Plough LTD and Schering-



Plough Corporation (collectively "Schering-Plough") and have received a milestone from Schering-Plough for nominating a compound as a clinical candidate. Additionally, we are conducting research on backup VLA-4 antagonists for Schering-Plough under this agreement.

- *Vascular Disease.* Many disease processes involve changes in blood vessels and heart tissue. There are numerous mediators, like endothelin, which may contribute to the development of these diseases. Several of these act through G-protein coupled receptors, GPCRs, to carry out their action. We are conducting research on urotensin and other GPCRs to identify inhibitors which could be useful in treating diseases including congestive heart failure, ("CHF"), ischemic stroke and acute myocardial infarction.

### **Business Strategy**

The key elements of our business strategy are as follows:

#### *Maximize sales of Argatroban*

Our marketing, manufacturing and distribution partner, GSK, began selling Argatroban in the U.S. during November 2000, and in Canada during June 2002, as an anticoagulant for prophylaxis or treatment of thrombosis in patients with HIT. In addition:

- during 2002, we received approval from the FDA on our supplementary New Drug Application ("sNDA") for Argatroban for use in patients, with or at risk for HIT, undergoing PCI;
- during 2002, GSK created a hospital based sales force and initiated programs to increase its sales efforts on Argatroban in the U.S. and Canada that could have a positive effect on our royalties from GSK;
- Argatroban is currently being evaluated, in a clinical trial, in combination with rt-PA as a new approach to the treatment of acute ischemic stroke by an investigator at the University of Texas Medical School at Houston. Argatroban is approved and sold in Japan by Mitsubishi Pharma Corporation ("Mitsubishi"), the licensor of Argatroban as mono-therapy for an indication of acute ischemic stroke; and
- we have completed initial studies to evaluate the use of Argatroban in hemodialysis patients and in PCI.

#### *Complete the clinical development of sitaxsentan and commercialize the compound worldwide*

We intend to initiate a pivotal Phase III clinical trial with sitaxsentan in 2003 with the goal of filing a new drug application with the FDA for use of sitaxsentan in patients with PAH. We intend to commercialize the compound on a worldwide basis by ourselves or through licensee arrangements:

- During 2002, ICOS-TBC completed a Phase I/II clinical trial to assess the safety and efficacy of sitaxsentan in patients with New York Heart Association ("NYHA") class II, III and IV PAH. Based on the results of this clinical trial and meeting with the FDA, TBC believes that development of sitaxsentan should be continued.
- In January 2003, ICOS announced that they had reached a conclusion that joint development of the endothelin receptor antagonist program, through ICOS-TBC, should not continue. ICOS has indicated that it is willing to transfer the endothelin antagonist program in its entirety, including sitaxsentan, to us. The financial terms of this transaction are subject to ongoing negotiations between the two companies. This will allow us to increase our ownership and the potential commercial benefit of the program from 50% to 100%.

#### *Focus on the identification and development of new drugs for the treatment of diseases involving the vascular endothelium*

Injury to the vascular endothelium is a common cause of many of the most profound diseases affecting patients today, such as ischemic heart disease, hypertension, congestive heart failure, and asthma. By concentrating on this area, we can be relatively efficient in our drug discovery, development and commercialization efforts. This efficiency extends to the following areas:

- Research — Our efforts are predominantly focused toward the treatment and prevention of interrelated diseases of the vascular endothelium, exploiting our research group's expertise in the area of vascular biology;
- Computer aided drug design — We utilize computers to rapidly develop drug candidates derived from our vascular biological efforts and to identify new targets from information discovered by the Human Genome Project; and
- Clinical investigators and consultants — We work with key opinion leaders and consultants experienced in vascular diseases to assist in clinical development, product planning and the regulatory approval process.

*Focus on the identification and development of small molecule drug candidates*

Synthetic, small molecule therapeutics have several advantages over protein and peptide based large molecules. Small molecules generally are not immunogenic, can typically be protected with composition-of-matter patents and can be produced by conventional lower cost pharmaceutical manufacturing methods.

*Participate in the sales and marketing in the United States and Canada of the drugs we develop*

In the biopharmaceutical industry, a substantial percentage of the profits generated from successful drug development are typically retained by the entity directly involved in the sales and marketing of the drug. Licensing our drug candidates to a third party who will complete development and provide sales and marketing resources in exchange for upfront payments, milestone payments and a royalty on sales may reduce some of our risks, particularly for diseases outside our strategic interest or in territories outside of the United States and Canada. In the future, however, we may decide that the risk-return profile favors developing and then marketing and selling products on a co-promotion basis or by ourselves. Therefore, when and if we deem it appropriate, we intend to participate in the sales and marketing of our products in the United States and Canada.

## Therapeutic Programs and Products in Development

The following table summarizes the potential therapeutic indications and development status for certain of our clinical, preclinical and research product candidates and is qualified in its entirety by the more detailed information appearing elsewhere in this Form 10-K.

Program	Target Compound/ Dose Form	Indication	Status(1)
Thrombosis	Argatroban Intravenous	Anticoagulant therapy for prophylaxis or treatment of patients with HIT	Marketed product
	Intravenous	Anticoagulant therapy for patients, with or at risk for HIT, undergoing PCI	Marketed product
Vasospasm/ Hypertension	<b>Endothelin (A) Receptor Antagonist</b> <i>Sitaxsentan (TBC11251)</i> Oral	Pulmonary Arterial Hypertension	Phase III
	<i>TBC3711</i> Oral	Pulmonary Arterial Hypertension	Phase I completed
	<b>Urotensin Receptor Antagonist</b>	Various	Research
	<b>Other GPCRs</b>	Various	Research
Vascular Inflammation	<b>Selectin Antagonist (being developed by Revotar)</b> <i>Bimosiamose (TBC1269)</i>		
	Inhaled	Asthma	Phase IIa
	Topical	Psoriasis and atopic dermatitis	Phase IIa
	<b>VCAM/VLA-4 Antagonist</b> <i>TBC4746</i> Oral	Asthma Multiple Sclerosis Rheumatoid Arthritis	Preclinical Preclinical Preclinical
	<b><math>\alpha 4\beta 7</math> Antagonist</b> <i>TBC3804</i> Oral	Inflammatory Bowel Disease	Research
<b>Other Cell Adhesion Molecules</b>	Various	Research	

- (1) Preclinical compounds are compounds undergoing toxicology and pharmaceutical development in preparation for human clinical testing. Research compounds are compounds undergoing basic evaluation and optimization to establish a lead clinical candidate.

## Thrombosis Program ARGATROBAN

*Background.* Thrombosis, the lodging of a blood clot in a vessel, causes various vascular diseases, depending on the location of the clot. An arterial clot may lead to heart attack if lodged in a coronary artery, or stroke if lodged in an artery that supplies oxygen to the brain. Venous clots occur principally in the arms or legs (deep vein thrombosis), and may cause local inflammation, chronic pain and other complications. In some cases, a venous clot can cause lung injury (pulmonary embolism) by migrating from the veins to the lungs.

Thrombosis can be treated surgically or through drug therapy with anticoagulant and thrombolytic drugs. Anticoagulant drugs prevent clots from forming. Heparin and aspirin are the most widely used antithrombotic drugs.

Heparin, first discovered over 80 years ago, is the most widely used injectable anticoagulant. In the U.S., approximately ten million patients annually receive therapeutic heparin to treat a variety of conditions that require inhibition of the body's natural clotting mechanism. Each year over 300,000 of these patients develop a profound immunological reaction to heparin that is known as heparin-induced thrombocytopenia. The condition is characterized by a paradoxical tendency to form clots. That puts the patient at risk of major complications such as acute myocardial infarction, ischemic stroke, amputation or death. It is also very difficult to administer heparin dosages.

*Current Therapies.* In conjunction with GSK, we obtained approval for Argatroban as an anticoagulant for prophylaxis or treatment of thrombosis in patients with HIT in the U.S. and Canada. GSK began marketing Argatroban in the U.S. in November 2000. Argatroban is a synthetic direct thrombin inhibitor that directly and selectively binds to and inactivates thrombin in the blood plasma. Argatroban is manufactured and marketed in Japan by Mitsubishi where it is approved as a treatment for ischemic stroke, peripheral arterial occlusion and hemodialysis in patients with antithrombin III deficiency, a clotting disorder that does not respond to heparin. Since the product's introduction in 1990, more than 200,000 patients have been treated with Argatroban in Japan. Other measures, such as inline filters, are sometimes used to remove clots, but are highly invasive and involve patient trauma. Simply stopping heparin alone may be insufficient, as a significant number of patients will progress to experience severe outcomes. Clinical studies that we conducted in the U.S. have shown a significant correlation between the administered dose of Argatroban and the degree of anticoagulation achieved. This is potentially important as it suggests that the relationship between dose and effect of Argatroban is generally very predictable over the expected dose-range. As a result, we believe there is little risk of either insufficient or excessive anticoagulation occurring from small dose changes of Argatroban. Other product advantages for Argatroban include a rapid onset of action, a relatively short half-life and an absence of immunogenicity.

*Clinical Trial Status.* During 2002, we completed a multi-center, placebo-controlled Phase II clinical trial (ARGIS-I) for the use of Argatroban, as monotherapy, in patients with ischemic stroke. During February 2003, we reported the Phase II trial results that met the primary endpoint related to safety. In light of a lack of an overall efficacy trend, and the high risk and high costs associated with stroke trials, it is unlikely that Texas Biotechnology will proceed independently with a full Phase III program. However, given the relatively positive safety outcome, and the high rate of stroke occurrence in HIT patients, some physicians may choose to use Argatroban in place of heparin in some patient populations. Currently, Argatroban is being evaluated in a clinical trial, in combination with rt-PA as a new approach to the treatment of acute ischemic stroke by an investigator at the University of Texas Medical School at Houston. Argatroban is approved and sold in Japan by Mitsubishi, the licensor of Argatroban, as mono-therapy for an indication of acute ischemic stroke. With GSK, we are conducting clinical trials to evaluate the use of Argatroban in hemodialysis patients and for use in PCI.

*Competition in HIT.* Primary competitors for Argatroban in its initial indication are Refludan<sup>®</sup> (lepirudin), marketed by Berlex Laboratories, Orgaran<sup>®</sup> (danaparoid sodium), manufactured by N.V. Organon, a unit of Akzo Nobel, and Angiomax<sup>®</sup> (bivalirudin) manufactured by The Medicines Company.

*Refludan<sup>®</sup> (lepirudin, Berlex).* This product received approval in Europe in 1997 and in the U.S. in 1998 for anticoagulation in patients with HIT to prevent further thromboembolic (clotting) complications. Refludan<sup>®</sup> has been associated with the development of an adverse immune response in up to 40% of patients receiving Refludan<sup>®</sup>. Several cases of anaphylaxis have been reported upon re-exposure to Refludan<sup>®</sup>. Although the full clinical impact of development of these antibodies is unknown, we understand that the anticoagulant effects of Refludan<sup>®</sup> may become

unpredictable in patients developing these antibodies. Additionally Recludan<sup>®</sup> is renally excreted while Argatroban is hepatically excreted. Berlex has stated they plan to submit for a HIT prevention label claim in the future.

*Orgaran<sup>®</sup> (danaparoid sodium, N.V. Organon).* This product is a low molecular weight heparinoid, a heparin-like compound extracted from pigs. The product was approved in the U.S. in 2001 for prevention of deep venous thrombosis following hip surgery. However, approximately one in ten HIT patients receiving Orgaran<sup>®</sup> will develop the HIT syndrome exactly as if the patient received heparin. Orgaran<sup>®</sup> is not approved in the U.S. for HIT and is used on an off-label basis only.

*Angiomax<sup>®</sup> (bivalirudin, The Medicines Company).* This product received approval in the U.S. in 2001 for use as an anticoagulant in patients with unstable angina undergoing percutaneous transluminal coronary angioplasty ("PTCA"). Angiomax<sup>®</sup> represents the third direct thrombin inhibitor approved in the U.S. Angiomax<sup>®</sup> is not approved for the treatment of HIT. The Medicines Company has stated their intention to expand the Angiomax<sup>®</sup> label to include the treatment and prevention of HIT.

*Other Indications.* Argatroban may be useful in other disease settings where predictable anticoagulation is desired. Argatroban may be effective in hemodialysis and PCI, particularly in patients who develop problems when given heparin.

*Competition for Argatroban in Other Indications.* Competitors for Argatroban in other applications include:

- Revasc<sup>®</sup> (desirudin, Aventis/Novartis A.G.), recombinant hirudin, is approved in Europe for the prevention of deep vein thrombosis following hip surgery, but has been associated with intracranial hemorrhage and antibody production;
- Melagatran (AstraZeneca plc) is in Phase III trials and is being developed as a treatment for deep vein thrombosis. They have stated that they intend to file an NDA during 2003; and
- Arixtra<sup>®</sup> (pentasaccharide, Sanofi-Synthelabo) was approved in the U.S. in 2002 for the prevention of deep vein thrombosis and pulmonary embolism.

## Vasospasm/Hypertension Program

*Background.* Smooth muscle cells in the blood vessel are responsible directly for mediating vessel diameter. The regulation of blood flow depends on a delicate balance between physical and chemical stimuli that cause smooth muscle cells to relax (vasodilatation) or contract (vasoconstriction). Chronic periods of excessive vasoconstriction in the peripheral circulation can lead to disturbances in blood pressure (hypertension) or heart function (congestive heart failure), whereas acute episodes of intense vasoconstriction (vasospasm) can restrict blood flow leading to severe tissue damage and organ failure (myocardial infarction or kidney failure). It has been determined that the vascular endothelium (innermost lining) plays a pivotal role in maintaining normal blood vessel tone, including blood flow, by producing substances that regulate the balance between vasodilatation and vasoconstriction.

Endothelin is a peptide that is believed to play a critical role in the control of blood flow. The action of endothelin can be explained by its interactions on cell surfaces with two distinct receptors, endothelin-A (ET<sub>A</sub>) and endothelin-B (ET<sub>B</sub>). In general, ET<sub>A</sub> receptors are associated with vasoconstriction, while ET<sub>B</sub> receptors are primarily associated with vasodilatation. There is substantial evidence that endothelin is involved in a variety of diseases where blood flow is important. These include vasospasm, congestive heart failure and certain types of hypertension.

Our research program in the vasospasm/hypertension area is aimed at developing small molecules that inhibit the binding of endothelin to its cell surface receptors. Our scientists believe that specific agents for each receptor subtype may provide the best clinical utility and safety. Our initial focus has been to develop a highly potent and selective small molecule based ET<sub>A</sub> receptor antagonist. An antagonist, or inhibitor, blocks the effects of a ligand at its receptor. A ligand is a chemical messenger, which binds to a specific site on a target molecule or cell. Our scientists have discovered a novel class of low molecular weight compounds that antagonize endothelin binding to the ET<sub>A</sub> receptor with high potency. We identified lead compounds which mimicked the ability of endothelin to bind to the ET<sub>A</sub> receptor. We then used further optimization techniques to develop more potent compounds until the current series of lead candidates were identified. In addition to their ability to block endothelin binding to its receptor, these compounds functionally inhibit endothelin action on isolated blood vessels *in vitro* acting as full, competitive antagonists. The lead compounds in this series have been shown to exhibit *in vivo* efficacy using various animal models. In addition, sitaxsentan and bosentan have demonstrated efficacy in human clinical trials, including patients with pulmonary hypertension.

*Current Therapies.* Current treatments for PAH remain unsatisfactory and new treatments are needed. At present, epoprostenol (Flolan<sup>®</sup> - GSK), bosentan (Tracleer<sup>®</sup> - Actelion), and treprostinil (Remodulin<sup>®</sup> - United Therapeutics) are approved treatments for patients with PAH.

Epoprostenol, a vasodilator requiring continuous infusion through a central venous catheter and special infusion pump, is costly, is associated with significant adverse events including those related to its delivery, and is typically reserved by clinicians for patients with NYHA functional class IV status. Bosentan, a nonselective ET-1 receptor antagonist, is the first oral agent approved for the treatment of PAH, and is indicated in patients with World Health Organization (WHO) functional class III and IV symptoms. Bosentan is also associated with significant potential for hepatotoxicity, teratogenicity, and reduction of male fertility. Treprostinil, a prostaglandin analog requiring administration through a chronic subcutaneous pump, is associated with a high incidence of local injection site reactions. A selective oral endothelin antagonist, if successful, may provide a significant benefit to these patients.

*Partnership.* During 2000, we formed ICOS-TBC, a partnership with ICOS, to co-develop and commercialize endothelin antagonist compounds. As part of the agreement, ICOS made an upfront payment and a milestone payment to ICOS-TBC, which in turn distributed these payments to TBC. In January 2003, ICOS announced that they had reached a conclusion that joint development of the endothelin receptor antagonist program, through ICOS-TBC should not continue. ICOS and TBC are currently negotiating the terms pursuant to which we could independently continue the program. The financial terms of this transaction are subject to ongoing negotiations between the two companies. This could allow us to increase our ownership and the potential commercial benefit of the program from 50% to 100%. The partners equally funded the cost of research and development through the end of 2002. After 2002, we are responsible for all costs of the program.

*Product Candidate — TBC11251 - Sitaxsentan.* The lead endothelin antagonist, sitaxsentan, is being developed for the indication of PAH. PAH is a disease with high mortality and an average survival time of approximately four

years from the time of diagnosis. Sitaxsentan, a highly selective endothelin-A receptor antagonist, may provide a distinct advantage over current therapies including the non-specific endothelin receptor antagonist Tracleer®.

*Clinical Trial Status.* —We filed an investigational new drug application, also referred to as an IND, with the FDA for sitaxsentan in late 1996. To date, three Phase IIa clinical trials have been completed, one in congestive heart failure patients, one in essential hypertension patients and one in pulmonary arterial hypertension patients. In a follow-on extension trial, treatment-related hepatitis was observed in two patients and one of these patients died. Following analysis of the open-label Phase IIa clinical trial and extension studies and discussions with the FDA, ICOS-TBC initiated a Phase IIb/III clinical trial (STRIDE) of sitaxsentan, at lower doses, for the treatment of PAH in the second quarter of 2001. During 2002, ICOS-TBC completed the STRIDE clinical trial to assess the safety and efficacy of sitaxsentan in patients with NYHA class II, III and IV pulmonary arterial hypertension. The trial enrolled 178 patients who were randomized to either sitaxsentan 100 mg, sitaxsentan 300 mg, or placebo treatment once a day.

The primary endpoint of the Phase IIb/III STRIDE trial was change in percent of predicted peak  $VO_2$  from baseline to week 12. The results showed a statistically significant improvement for the 300 mg dose group compared with placebo treatment (7% relative improvement). The primary endpoint was not statistically significant for the 100 mg dose group. A secondary endpoint was change in 6-minute walk distance from baseline to week 12. The results showed statistically significant improvement for both the sitaxsentan 100 mg and 300 mg groups, compared with placebo treatment. The 6-minute walk test is the most widely used efficacy test for drugs treating PAH. The clinical effectiveness of each of the two sitaxsentan dose groups was equivalent for 6-minute walk distance (9% relative improvement). NYHA class improvement, another important measure that reflects limitations in physical activity, was also statistically significant for the sitaxsentan 100 mg and 300 mg dose groups compared with placebo treatment.

Based on the results of this clinical trial and meeting with the FDA, TBC believes that development of sitaxsentan should be continued. Based on concerns the FDA has raised regarding the class, such as hepatic toxicity and reproductive abnormalities, which may or may not be associated with our compounds, we are pursuing indications with unmet medical needs such as PAH.

*Product Candidate — TBC3711.* TBC3711 is our second endothelin antagonist compound and has been selected as the next clinical candidate. We believe TBC3711 is more selective and more potent than sitaxsentan and that a potential market opportunity for TBC3711 exists for the treatment of PAH and other diseases. ICOS-TBC has completed Phase I clinical studies with TBC3711 and is evaluating the development plan for the compound.

*Other Indications.* We believe endothelin antagonist compounds may provide therapeutic value in several other indications.

*Competition.* A number of companies including Abbott Laboratories, and Myogen, Inc., have  $ET_A$  receptor selective antagonist compounds in clinical development.  $ET_{(A)}$  receptor-selective compounds from Abbott are in early Phase III development. They have reported mixed results from a Phase III trial in severe hormone resistant prostate cancer patients. The compound reduced pain and PSA levels, but failed to delay disease progression. They are conducting additional studies in other cancer groups. Myogen has begun a Phase IIa trial for their  $ET_A$  compound in PAH. We believe our compounds are competitive with those from the other companies in terms of bioavailability (how much reaches the appropriate body system), half-life (how long the drugs last in the body) and potency. Several companies have non-selective endothelin antagonists in development. Actelion Ltd., a biotechnology company located in Switzerland, and Genentech, Inc. received approval from the FDA to market Tracleer® (bosentan) for the treatment of PAH during 2001. We believe that selective endothelin blockers like sitaxsentan will be preferred by physicians since selective  $ET_A$  blockers block the negative effects of endothelin at the  $ET_A$  receptor, and do not block the beneficial effects of endothelin at the  $ET_B$  receptor. Non-selective antagonists block both the  $ET_A$  and the  $ET_B$  receptors. Abbott/Knoll's development of darusentan and Actelion's development of Tracleer® for heart failure have generated negative data. It is not known if the negative clinical data is due to a class effect, trial design or specific to the compounds themselves.

In addition to endothelin antagonists, Pfizer is conducting a Phase II trial in the use of Viagra® in PAH. If phosphodiesterase 5 inhibitors ("PDE-5 inhibitor") demonstrate a benefit in PAH patients, we believe they will be used as additive therapy with endothelin antagonists.

## Vascular Inflammation Program

*Background.* Inflammation is the body's natural defense mechanism that fends off bacterial, viral and parasitic infections. The inflammatory response involves a series of events by which the body attempts to limit or destroy a foreign agent. These steps include the production of proteins that attract white blood cells, or leukocytes, to the site of inflammation, the production of chemicals to destroy the foreign agent and the removal of the resulting debris. This process is normally self-limiting and not harmful to the individual. However, in certain instances, the process may be overly active, such as during an acute asthma attack where an immediate inflammatory reaction occurs. In addition, in diseases such as atherosclerosis or rheumatoid arthritis, the inflammatory reaction leads to a build up of white blood cells and debris at the inflammation site that causes tissue damage over longer periods of time.

The initial interaction between white blood cells and the endothelial cell layer is mediated by a group of adhesion molecules known as selectins. The selectins are a family of three proteins, two of which are found on inflamed endothelium, which bind to the carbohydrate sialyl Lewis x, also referred to as sLe(X), found on the surface of white blood cells. White blood cells are able to migrate into inflamed areas because sLe(X) present on the surface of white blood cells binds to selectin molecules present on activated endothelium. This binding slows the flow of white blood cells or leukocytes through the bloodstream. This is one of the first steps in the movement of white blood cells from the blood into the tissue. The second step in this process is vascular cell adhesion molecule, referred to as VCAM, mediated white blood cell attachment and migration which helps to localize white blood cells in areas of injury or infection. The presence of VCAM at sites of endothelial injury leads to an accumulation at these sites of the integrin very late antigen-4, or VLA-4, which are contained in white blood cells. Such accumulation can provoke an inflammatory response.

*Current Therapies.* The major anti-inflammatory compounds are corticosteroids, leukotriene blockers and immunosuppressants such as cyclosporin. While effective, the time to onset of action of these compounds may be significant. Corticosteroids also have significant side effects including growth suppression in children, cataract formation, and general intolerance. The antagonist compounds we are developing may provide efficacy with fewer of these side effects.

*Product Candidate* — Bimosiamose is being developed by Revotar, our majority owned affiliate. Our scientists have developed a computer model of the selectin/sLe(X) complex and used it to produce a novel class of synthetic, small molecule compounds that inhibit the selectin-mediated cellular adhesion that occurs during inflammation. The lead compound in the series, bimosiamose, has shown efficacy both in cell-based and biochemical assays, and in animal models of inflammation. A Phase IIa clinical trial for bimosiamose's intravenous use in asthma was completed in 1998. Results of this trial, which involved 21 patients, demonstrated significant reductions in cellular inflammation and allowed improved breathing. The inhaled form of bimosiamose has been tested in Phase I clinical trials completed during 2001 for the treatment of asthma and a Phase IIa clinical trial was completed and showed signs of activity, utilizing an injectable form of bimosiamose as a proof-of-concept for psoriasis. During 2002, Revotar began a Phase II clinical trial in asthma, utilizing the inhaled form and intends to commence a Phase IIa clinical trial in psoriasis utilizing the topical form during 2003.

*German Affiliate* — *Revotar Biopharmaceuticals, AG.* During 2000, Revotar Biopharmaceuticals, AG, a German affiliate, was formed and we retained a 55.2% ownership percentage. With headquarters in Berlin, Germany, Revotar was formed to perform research and development of novel small molecule compounds and to develop and commercialize selectin antagonists that TBC licensed to Revotar. Upon formation, Revotar received certain development and commercialization rights to the Company's selectin antagonist compounds as well as rights to certain other TBC research technology for use in certain territories. Revotar also received approximately \$5 million in funding from three German venture capital funds and has access to certain German government scientific grants. During 2001, Revotar entered into a research agreement regarding macrophage migration inhibitory factor (MIF) with the Fraunhofer Institute in Stuttgart, Germany. We amended our license and research agreement with Revotar during 2003 to better reflect the commercial priorities of each company. Under the amended agreement, Revotar will have exclusive worldwide rights to bimosiamose for the treatment of asthma and other inflammatory indications as well as rights outside of North America for topical indications. Texas Biotechnology will have exclusive worldwide rights for the use of bimosiamose in organ transplant as well as exclusive North American rights to all topical indications. Under the amended agreement, each party has certain revenue sharing and royalty obligations. In 2002, the stockholders of Revotar executed an agreement to provide approximately \$4.5 million in unsecured loans, of which our commitment was approximately \$3.4 million. Under the loan agreement, we have advanced approximately \$1.2



million to Revotar during 2002. We believe that Revotar's existing funds, the remaining commitments under the loan agreement and proceeds under German government scientific grants will be sufficient to fund Revotar into the first quarter of 2004. In order to continue to operate beyond that time, Revotar will need to seek additional funding through collaborative arrangements and/or through public or private financings in the future.

*Clinical Trial Status.* — The inhaled form of bimosiamose has been tested by Revotar in Phase I clinical trials completed during 2001 for the treatment of asthma and a Phase IIa clinical trial was completed in Germany utilizing an injectable form of bimosiamose as a proof-of-concept for psoriasis. During 2002, Revotar began a Phase IIa clinical trial in asthma, utilizing the inhaled form and intends to initiate a Phase IIa clinical trial in psoriasis utilizing the topical form during 2003.

*Product Candidate — VCAM/VLA-4 Antagonists.* We have also identified antagonists for the VCAM-dependent intercellular adhesion observed in asthma, which blocks the ability of white blood cells to interact through VCAM and VLA-4. VLA-4 antagonists represent a new class of compounds that has shown promise in multiple preclinical animal models of asthma. These lead compounds are being modified in an attempt to develop an orally available clinical candidate. In preclinical animal studies, our scientists have demonstrated that a small molecule VLA-4 antagonist can be effective in blocking acute inflammation, suggesting that VCAM/VLA-4 plays a role in this disease process. During 2002, TBC4746 was nominated as a clinical candidate and pursuant to our agreement with Schering-Plough, we received a milestone payment.

*Product Candidate —  $\alpha 4\beta 7$  Antagonists.* The integrin  $\alpha 4\beta 7$ , which is closely related to VLA-4, is present on leukocytes which locate in the gastrointestinal system. Inhibitors of  $\alpha 4\beta 7$  may be useful in treating inflammatory conditions of the gut such as inflammatory bowel disease (estimated 300,000 U.S. patients).

*Research Collaboration with Schering-Plough.* — On June 30, 2000, we entered into a worldwide research collaboration and license agreement to discover, develop and commercialize VLA-4 antagonists with Schering-Plough. The primary focus of the collaboration will be to discover orally available VLA-4 antagonists as treatments for asthma. Under the terms of the agreement, Schering-Plough obtains the exclusive worldwide rights to develop, manufacture and market all compounds from TBC's library of VLA-4 antagonists, as well as the rights to a second integrin antagonist. TBC is responsible for optimizing a lead compound and additional follow-on compounds. Schering-Plough is supporting research at TBC and will be responsible for all costs associated with the worldwide product development program and commercialization of the compound. In addition to reimbursing research costs, Schering-Plough paid an upfront license fee and will pay development milestones and royalties on product sales resulting from the agreement. Total payments to TBC for both the VLA-4 and an additional program, excluding royalties, could reach \$87.0 million. During 2002, TBC4746 was nominated as a clinical candidate and pursuant to our agreement with Schering-Plough, we received a milestone payment.

*Competition.* Several companies have programs aimed at inhibiting cell adhesion molecules and integrins, like  $\alpha 4\beta 7$  and VCAM/VLA-4. We are not aware of any competing product antagonists of these classes, which are currently in clinical development. While no oral VCAM/VLA-4 inhibitors are in clinical development, Biogen, Inc. and Elan Corporation plc have obtained positive Phase II data with Antegren<sup>®</sup>, a monoclonal antibody against VLA-4, in multiple sclerosis and inflammatory bowel disease. They are planning to conduct Phase III studies with this product.

### *Vascular Disease*

*Background and current status.* Many disease processes involve changes in blood vessels and heart tissue. There are numerous mediators, like endothelin, which may contribute to the development of these diseases. Several of these act through G-protein coupled receptors, GPCRs, to carry out their action. We are conducting research on urotensin and other GPCRs to identify inhibitors which could be useful in treating diseases including CHF, ischemic stroke and acute myocardial infarction. There are numerous companies studying these and other GPCRs. We believe our projects are competitive with these other programs.

## Research and Development Collaborations and Licensing Agreements

We have established, and intend to continue to establish, collaborations with a number of corporations, research institutions and scientists to further our research and development objectives and expedite the commercialization of our products. Our major licensing and collaboration agreements are summarized below:

*Mitsubishi Pharma Corporation ("Mitsubishi").* We entered into an agreement with Mitsubishi to license Mitsubishi's rights and technology relating to Argatroban and to license Mitsubishi's own proprietary technology developed with respect to Argatroban (the "Mitsubishi Agreement"). Under the agreement with Mitsubishi, we have an exclusive license to use and sell Argatroban in the U.S. and Canada for all cardiovascular, renal, neurological and immunological purposes other than use for the coating of stents. We are required to pay Mitsubishi specified royalties on net sales of Argatroban by us and our sublicensees after its commercial introduction in the U.S. and Canada. Either party may terminate the agreement with Mitsubishi on 60 days notice if the other party defaults in its material obligations under the agreement, declares bankruptcy or becomes insolvent, or if a substantial portion of its property is subject to levy. Unless terminated sooner, the agreement with Mitsubishi expires on the later of termination of patent rights in a particular country or 20 years after first commercial sale of products in a particular country. Under the Mitsubishi Agreement, we have access to an improved formulation patent granted in the U.S. in 1993, which expires in 2010, and a use patent in the U.S., which expires in 2009. We have agreed to pay a consultant involved in the negotiation of this agreement a royalty based on net sales of Argatroban. During 2000, we signed an additional agreement with Mitsubishi that provides us with royalties on sales of Argatroban in certain European countries, up to a total of \$5.0 million in milestones for the development of ischemic stroke and certain other provisions. During 2001, we received \$2.0 million of these milestones less certain Japanese withholding taxes. Additional milestones are dependent on further development of Argatroban in the indication of ischemic stroke. During 2002, we completed a Phase II human clinical trial for Argatroban as a monotherapy treatment for acute ischemic stroke. The clinical trial met the primary safety endpoint and showed positive results in the secondary safety endpoint. In light of a lack of an overall efficacy trend and the high risk and high costs associated with stroke trials, it is unlikely that we will proceed independently with a full Phase III program.

*GlaxoSmithKline.* In connection with our development and commercialization of Argatroban, on August 5, 1997, we entered into an agreement with GSK whereby GSK was granted an exclusive sublicense in the U.S. and Canada for the indications of Argatroban that we have licensed from Mitsubishi. GSK has paid \$8.5 million in upfront license fees and \$12.5 million in milestone payments and has agreed to pay up to an additional \$7.5 million in additional milestone payments based on the clinical development and FDA approval of Argatroban for the acute myocardial infarction indication. We are evaluating the feasibility of development of Argatroban for other indications including use in hemodialysis and PCI.

The agreement with GSK provides for the formation of a joint development committee to analyze the development of additional Argatroban indications (such as PCI) covered by our license from Mitsubishi. The joint development is to be funded 60% by GSK, except Phase IV trials are paid 100% by GSK. Except as discussed below, GSK has the exclusive right to commercialize all products arising out of the collaboration, subject to the obligation to pay royalties on net sales to us and our rights to co-promote these products through our own sales force in certain circumstances. We will retain the rights to any indications that GSK determines it does not wish to pursue (such as ischemic stroke), subject to the requirement that we may not grant marketing rights to any third parties, and must use our own sales force to commercialize any such indications. Any indications that GSK and TBC elect not to develop will be returned to Mitsubishi, subject to the rights of GSK and TBC to commercialize these indications at TBC's election, with GSK having the first opportunity to commercialize. Mitsubishi may also request the joint development committee to develop new indications inside or outside the licensed field of use, and if the joint development committee determines that it does not want to proceed with any such indication, all rights under the agreement with Mitsubishi regarding such indication will revert to Mitsubishi subject to our and GSK's right to commercialize the indication, with GSK having the first opportunity to commercialize.

The agreement with GSK generally terminates on a country-by-country basis upon the earlier of the termination of our rights under the agreement with Mitsubishi, the expiration of applicable patent rights, or in the case of certain royalty payments, the commencement of substantial third-party competition. GSK also has the right to terminate the agreement on a country by country basis by giving us at least three months written notice that the commercial profile of the product in question would not justify continued development or marketing in that country. In addition, either party may terminate the agreement on 60 days notice if the other party defaults in its obligations under the agreement,

declares bankruptcy or becomes insolvent. We agreed to pay an agent involved in the negotiation of this agreement a fee based on a percentage of all consideration we receive, including royalties, from sales of Argatroban.

At present, Mitsubishi is the only manufacturer of Argatroban, and has entered into an agreement with GSK to supply Argatroban in bulk to meet GSK's needs. Should Mitsubishi fail during any consecutive nine-month period to supply GSK at least 80% of its requirements, and such requirements cannot be satisfied by existing inventories, the agreement provides for the nonexclusive transfer of the production technology to GSK. If GSK cannot commence manufacturing of Argatroban in a timely manner or if alternate sources of supply are unavailable or uneconomical, our results of operations would be harmed. GSK has informed us that they will be finishing and packaging in a GSK facility in the future.

In connection with the execution of our agreement with GSK, GSK purchased 176,922 shares of common stock for \$1.0 million and an additional 400,000 shares of common stock for \$2.0 million in connection with the secondary public offering, which closed on October 1, 1997.

*ICOS-TBC L.P.* In June 2000, we entered into a limited partnership agreement with ICOS to form ICOS-TBC. The partnership was formed to develop and globally commercialize endothelin-A receptor antagonists from the TBC endothelin antagonist program. ICOS-TBC has made an upfront license fee payment and milestone payment for the development and commercialization of products resulting from the collaboration and the partners equally funded the cost of research and development through the end of 2002. In January 2003, ICOS announced that they had reached a conclusion that joint development of the endothelin receptor antagonist program, through ICOS-TBC should not continue. ICOS and TBC are currently negotiating the terms pursuant to which TBC could independently continue the program. The financial terms of this transaction are subject to ongoing negotiations between the two companies. If TBC is successful in obtaining 100% ownership of the program, TBC's share of the costs and potential commercial benefit of the program will increase from 50% to 100%. See Note 8 to the Consolidated Financial Statements for a discussion of this transaction.

*Schering-Plough.* In June 2000, TBC and Schering-Plough entered into a worldwide research collaboration and license agreement to discover, develop and commercialize VLA-4 antagonists, with Schering-Plough having rights to a second integrin antagonist target. In addition to funding research costs, Schering-Plough paid TBC an upfront license fee and milestone payment, and will pay us additional development milestones and royalties on product sales resulting from the agreement. Total payments to us for both programs, excluding royalties, could reach \$87.0 million. See Note 8 to the Consolidated Financial Statements for a discussion of this transaction.

*Revotar Biopharmaceuticals, AG.* During September 2000, Revotar was formed and we transferred to Revotar certain development and commercialization rights to our selectin antagonist program as well as rights to other proprietary technology. See Note 9 to the Consolidated Financial Statements for a discussion of this transaction. The primary focus of Revotar has been on the design and initiation of a Phase I trial for bimosiamose using the inhaled formulation of the drug, which was completed during 2001. During 2002, Revotar began a Phase IIa clinical trial in asthma, utilizing the inhaled form and intends to commence a Phase IIa clinical trial in psoriasis utilizing the topical form in 2003.

#### Licenses and Patents

Because of the substantial length of time and expense associated with developing new pharmaceutical products, the biotechnology industry places considerable importance on obtaining patent and trade secret protection for new technologies, products and processes. Our policy is to file patent applications to protect technology, inventions and improvements that are important to the development of our business. We have 18 pending U.S. patent applications and 34 issued U.S. patents covering compounds including selectin inhibitors, endothelin antagonists and VCAM/VLA-4 antagonists. In addition, we have exclusive licenses to three patents covering rational drug design technology. We have also filed patent applications in certain foreign jurisdictions covering projects that are the subject of U.S. applications and intend to file additional patent applications as our research projects develop.

We in-licensed the U.S. and Canadian rights to Argatroban in 1993, which included access to an improved formulation patent granted in 1993, which expires in 2012, and a use patent for the use of Argatroban as a fibrinolysis-enhancing agent, which expires in 2009. The Mitsubishi composition of matter patent on Argatroban has expired. We have access to other patents held by Mitsubishi, however, these are not being utilized currently.

Argatroban received FDA approval on June 30, 2000. We currently market Argatroban and enjoy market exclusivity pursuant to the Waxman/Hatch Act that provides protection from competition until June 30, 2005. We can obtain an extension under Waxman/Hatch until December 31, 2005 under certain circumstances pertaining to submission of pediatric data. Argatroban is currently marketed in a formulation that is covered under a formulation patent that expires in 2010. We will also be submitting a process patent, that expires in 2019, to the FDA for inclusion in the FDA Orange Book of Approved Drug Products. Following expiration of Waxman/Hatch protection, it is possible that generic manufacturers may be able to produce Argatroban without violating the formulation or process patents.

The patent positions of biopharmaceutical firms, including us, are uncertain and involve complex legal and factual questions. Consequently, we do not know whether any of our applications will result in the issuance of patents or, if any patents are issued, whether they will provide significant proprietary protection or will be circumvented or invalidated. Since patent applications in the U.S. are maintained in secrecy until patents issue, and since publication of discoveries in the scientific or patent literature often lags behind actual discoveries, we cannot be certain that we were the first creator of inventions covered by our pending patent applications or that we were the first to file patent applications for such inventions. Moreover, we may have to participate in interference proceedings declared by the U.S. Patent and Trademark Office, commonly known as the PTO, to determine priority of invention, which could result in substantial cost to us, even if the eventual outcome is favorable to us. We have no interference proceedings pending which involve compounds currently of commercial interest to us. We cannot assure you that our patents, if issued, would be held valid by a court of competent jurisdiction. An adverse outcome could subject us to significant liabilities to third parties, require disputed rights to be licensed from third parties or require us to cease using such technology.

The development of therapeutic products for cardiovascular applications is intensely competitive. Many pharmaceutical companies, biotechnology companies, universities and research institutions have filed patent applications or received patents in this field. Some of these applications or patents may be competitive with our applications or conflict in certain respects with claims made under our applications. Such conflict could result in a significant reduction of the coverage of our patents, if issued. In addition, if patents are issued to other companies that contain competitive or conflicting claims and such claims are ultimately determined to be valid, we cannot assure you that we would be able to obtain licenses to these patents at a reasonable cost or develop or obtain alternative technology.

We also rely upon trade secret protection for our confidential and proprietary information. We cannot assure you that others will not independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose such technology, or that we can meaningfully protect our trade secrets.

We require our employees, consultants, members of our scientific advisory board, outside scientific collaborators and sponsored researchers and certain other advisors to enter into confidentiality agreements with us that contain assignment of invention clauses. These agreements provide that all confidential information developed or made known to the individual during the course of the individual's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of our employees, the agreements provide that all inventions conceived by the employee are our exclusive property. We cannot assure you, however, that these agreements will provide meaningful protection or adequate remedies for our trade secrets in the event of unauthorized use or disclosure of such information.

#### **Government Regulation**

The research, testing, manufacture and marketing of drug products are extensively regulated by numerous governmental authorities in the United States and other countries. In the United States, drugs are subject to rigorous regulation by the FDA. The Federal Food, Drug and Cosmetic Act, and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, record keeping, labeling, promotion and marketing and distribution of pharmaceutical products. Failure to comply with applicable regulatory requirements may subject a company to administrative or judicially imposed sanctions such as:

- warning letters;
- civil penalties;

- criminal prosecution;
- injunctions;
- product seizure;
- product recalls;
- total or partial suspension of production; and
- FDA refusal to approve pending New Drug Application (“NDA”) applications or NDA supplements to approved applications.

The steps ordinarily required before a new pharmaceutical product may be marketed in the United States include:

- preclinical laboratory tests, animal tests and formulation studies;
- the submission to the FDA of an IND, which must become effective before clinical testing may commence;
- adequate and well-controlled clinical trials to establish the safety and effectiveness of the drug for each indication;
- the submission of an NDA to the FDA; and
- FDA review and approval of the NDA prior to any commercial sale or shipment of the drug.

Preclinical tests include laboratory evaluation of product chemistry and formulation, as well as animal trials to assess the potential safety and efficacy of the product. Preclinical tests must be conducted in compliance with Good Laboratory Practice guidelines and compounds for clinical use must be formulated according to compliance with Good Manufacturing Practice, or cGMP, requirements. The results of preclinical testing are submitted to the FDA as part of the IND and NDA.

A 30-day waiting period after the filing of each IND is required prior to the commencement of clinical testing in humans. If the FDA has not commented on or questioned the IND within this 30-day period, clinical trials may begin. If the FDA has comments or questions, the questions must be answered to the satisfaction of the FDA before initial clinical testing can begin. In addition, the FDA may, at any time, impose a clinical hold on ongoing clinical trials. If the FDA imposes a clinical hold, clinical trials cannot commence or recommence without FDA authorization and then only under terms authorized by the FDA. In some instances, the IND application process can result in substantial delay and expenses.

Clinical trials involve the administration of the investigational new drug to healthy volunteers or patients under the supervision of a qualified principal investigator. Clinical trials are conducted in accordance with Good Clinical Practice guidelines, under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND. The study protocol and informed consent information for patients in clinical trials must also be approved by the institutional review board at each institution where the trials will be conducted.

Clinical trials to support NDAs are typically conducted in three sequential phases, which may overlap. In Phase I, the initial introduction of the drug into healthy human subjects or patients, the drug is tested to assess metabolism, pharmacokinetics and pharmacological actions and safety, including side effects associated with increasing doses. Phase II usually involves trials in a limited patient population to:

- determine dosage tolerance and optimal dosage;
- identify possible adverse effects and safety risks; and
- preliminarily support the efficacy of the drug in specific, targeted indications.

If a compound is found to be effective and to have an acceptable safety profile in Phase II evaluation, Phase III trials are undertaken to further evaluate clinical efficacy and to further test for safety within an expanded patient population at geographically dispersed clinical trial sites. There can be no assurance that Phase I, Phase II or Phase III testing of our product candidates will be completed successfully within any specified time period, if at all.

After completion of the required clinical testing, generally an NDA is prepared and submitted to the FDA. FDA approval of the NDA is required before marketing may begin in the United States. The NDA must include the results of extensive clinical and other testing and the compilation of data relating to the product's chemistry, pharmacology and manufacture. The cost of an NDA is substantial.

The FDA has 60 days from its receipt of the NDA to determine whether the application will be accepted for filing based on the threshold determination that the NDA is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Currently, for a standard review, the FDA takes approximately twelve months in which to review the NDA and respond to the applicant. In 1997, Congress enacted the Food and Drug Administration Modernization Act, in part, to ensure the availability of safe and effective drugs by expediting the FDA review process for certain new products. This act establishes a statutory program for the approval of fast track products (those drugs which address unmet medical needs for serious and life-threatening conditions). Under this act, the FDA has six months in which to review the NDA and respond to the applicant. The review process is often significantly extended by FDA requests for additional information or clarification regarding information already provided in the submission. The FDA may refer the application to the appropriate advisory committee, typically a panel of clinicians, for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee.

If FDA evaluations of the NDA and the manufacturing facilities are favorable, the FDA may issue an approval letter, or, in some cases, an approvable letter followed by an approval letter. The approvable letter may contain a number of conditions that must be met in order to secure final approval of the NDA. When and if those conditions have been met to the FDA's satisfaction, the FDA will issue an approval letter. The approval letter authorizes commercial marketing of the drug for specific indications. As a condition of NDA approval, the FDA may require post-marketing testing and surveillance to monitor the drug's safety or efficacy, or impose other conditions, commonly referred to as Phase IV trials.

If the FDA's evaluation of either the NDA submission or manufacturing facilities is not favorable, the FDA may refuse to approve the NDA or issue a not approvable letter. The not approvable letter outlines the deficiencies in the submission and often requires additional testing or information. Notwithstanding the submission of any requested additional data or information in response to an approvable or not approvable letter, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems occur following initial marketing.

*Manufacturing.* Each domestic drug manufacturing facility must be registered with FDA. Domestic drug manufacturing establishments are subject to periodic inspection by the FDA and must comply with cGMP. Further, we or our third party manufacturer must pass a preapproval inspection of its manufacturing facilities by the FDA before obtaining marketing approval of any products. To supply products for use in the United States, foreign manufacturing establishments must comply with cGMP and are subject to periodic inspection by the FDA or corresponding regulatory agencies in countries under reciprocal agreements with the FDA. We use and will continue to use third party manufacturers to produce our products in clinical and commercial quantities. There can be no guarantee that future FDA inspections will proceed without any compliance issues requiring the expenditure of money or other resources.

*Foreign Regulation of Drug Compounds.* Whether or not FDA approval has been obtained, approval of a product by comparable regulatory authorities is necessary in foreign countries prior to the commencement of marketing of the product in those countries. The approval procedure varies among countries and can involve additional testing. The time required may differ from that required for FDA approval. Although there are some procedures for unified filings for some European countries with the sponsorship of the country which first granted marketing approval, in general each country has its own procedures and requirements, many of which are time consuming and expensive. Thus, there can be substantial delays in obtaining required approvals from foreign regulatory authorities after the relevant applications are filed.

In Europe, marketing authorizations may be submitted at a centralized, a decentralized or a national level. The centralized procedure is mandatory for the approval of biotechnology products and provides for the grant of a single

marketing authorization, which is valid in all European Union member states. As of January 1995, a mutual recognition procedure is available at the request of the applicant for all medicinal products, which are not subject to the centralized procedure. We will choose the appropriate route of European regulatory filing to accomplish the most rapid regulatory approvals. There can be no assurance that the chosen regulatory strategy will secure regulatory approvals on a timely basis or at all.

*Hazardous Materials.* Our research and development processes involve the controlled use of hazardous materials, chemicals and radioactive materials and produce waste products. We are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of hazardous materials and waste products. Although we believe that our safety procedures for handling and disposing of hazardous materials comply with the standards prescribed by laws and regulations, the risk of accidental contamination or injury from these materials cannot be eliminated completely. In the event of an accident, we could be held liable for any damages that result. This liability could exceed our resources or not be covered by our insurance. Although we believe that we are in compliance in all material respects with applicable environmental laws and regulations, there can be no assurance that we will not be required to incur significant costs to comply with environmental laws and regulations in the future. There can also be no assurance that our operations, business or assets will not be materially adversely affected by current or future environmental laws or regulations.

### **Competition**

The development and sale of new drugs for the treatment of vascular and inflammatory diseases is highly competitive and we will face intense competition from major pharmaceutical companies and biotechnology companies all over the world. Competition is likely to increase as a result of advances made in the commercial application of technologies and greater availability of funds for investment in these fields. Companies that complete clinical trials, obtain required regulatory approvals and initiate commercial sales of their products before their competitors may achieve a significant competitive advantage. In addition, significant research in biotechnology and vascular medicine may occur in universities and other nonprofit research institutions. These entities have become increasingly active in seeking patent protection and licensing revenues for their research results. They also compete with us in recruiting talented scientists and business professionals.

We believe that our ability to compete successfully will depend on our ability to create and maintain scientifically-advanced technology, develop proprietary products, attract and retain scientific and other personnel, obtain patent or other protection for our products, obtain required regulatory approvals and manufacture and successfully market products through other companies, through co-promotion agreements or alone. Many of our competitors have substantially greater financial, marketing, and human resources than we do. We expect to encounter significant competition.

### **Manufacturing and Marketing**

We rely on our internal resources and third-party manufacturers to produce compounds for preclinical development. Currently, we have no manufacturing facilities for either the production of biochemicals or the manufacture of final dosage forms. We believe small molecule drugs are less expensive to manufacture than protein-based therapeutics, and that all of our existing compounds can be produced using established manufacturing methods, including traditional pharmaceutical synthesis.

We have established supply arrangements with third-party manufacturers for certain clinical trials and have established and will establish supply arrangements ultimately for commercial distribution, although there can be no assurance that such arrangements will be established on reasonable terms. Our long-range plan may involve establishing internal manufacturing of small molecule therapeutics, including the ability to formulate, fill, label, package and distribute our products. However, for the foreseeable future we plan to outsource such manufacturing. We do not anticipate developing an internal manufacturing capability for some time, nor are we able to determine which of our potential products, if any, will be appropriate for internal manufacturing. The primary factors we will consider in making this determination are the availability and cost of third-party sources, the expertise required to manufacture the product and the anticipated manufacturing volume. Pursuant to our agreement with GSK, GSK entered into an agreement with Mitsubishi regarding the manufacture and supply of Argatroban, and we will not, therefore, have any direct responsibility regarding the manufacture and supply of Argatroban as it relates to the agreement with GSK.

## Employees

As of December 31, 2002, we employed 104 individuals. During January 2003, we implemented a restructuring plan that reduced our work force to 82. Of our restructured work force, 66 employees are engaged directly in research and development activities and 16 in general and administrative positions. None of our employees are represented by a labor union. We have experienced no work stoppages and believe that relations with our employees are good. We also maintain consulting agreements with a number of scientists at various universities and other research institutions.

## Consultants and Scientific Advisors

We have assembled a scientific advisory board composed of distinguished professors from some of the most prestigious medical schools. The scientific advisory board assists us in identifying research and development opportunities, in reviewing with management the progress of our projects and in recruiting and evaluating scientific staff. Although we expect to receive guidance from the members of our scientific advisory board, all of its members are employed on a full-time basis by others and, accordingly, are able to devote only a small portion of their time to us. Management expects to meet with its scientific advisory board members as a group approximately once each year and individually from time to time on an informal basis. We have entered into a consulting agreement with each member of the scientific advisory board. The Scientific Advisory Board includes James T. Willerson, M.D., as Chairman, and the following scientists.

*Ferid Murad, M.D., Ph.D.* is Professor and Chairman of the Department of Integrative Biology and Pharmacology at the University of Texas-Houston Medical School and the Director of the Institute of Molecular Medicine. Dr. Murad has received many honors including the Nobel Prize in Medicine in 1998, the Ciba Award in 1988 and the Albert and Mary Lasker Award in Basic Medical Research in 1996. He is also a member of many professional and honorary societies and is the author or co-author of more than 300 scientific articles.

*Ajit Varki, M.D.* has been a Professor of Medicine since 1991 and is currently serving in that position as well as leader of the glycobiology program at the University of California, San Diego. Dr. Varki served as Instructor in Medicine at Washington University School of Medicine from 1980 to 1982. He also served as Assistant Professor of Medicine from 1982 to 1987 and as Associate Professor of Medicine from 1987 to 1991 at the University of California, San Diego. In 1975, Dr. Varki received an M.D. from Christian Medical College and his Post-Doctorate in Biochemistry from Washington University from 1979 to 1982. He is a member of various professional societies and has won numerous awards since 1969. He is currently president of the American Society for Clinical Investigation. Dr. Varki is the author or co-author of 160 scientific publications.

*Denton Cooley, M.D.*, Surgeon-in-Chief of the Texas Heart Institute, acts as an advisory director to us.

We also have agreements with various outside scientific consultants who assist us in formulating our research and development strategy. All of our consultants and advisors are employed by other employers and may have commitments to or consulting or advisory contracts with other entities that may affect their ability to work with us.

## Internet Website

Our Internet website can be found at [www.tbc.com](http://www.tbc.com). We make available free of charge, or through the "Investor Relations" section of our Internet website at [www.tbc.com](http://www.tbc.com), access to our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed pursuant to Section 13(a) or 15(d) of the Exchange Act as soon as reasonably practicable after such material is filed, or furnished to the Securities and Exchange Commission.



## ADDITIONAL RISK FACTORS

*Stockholders and potential investors in shares of our stock should carefully consider the following risk factors, in addition to other information in this Form 10-K. We are identifying these risk factors as important factors that could cause our actual results to differ materially from those contained in any written or oral forward-looking statements made by or on behalf of us. We are relying upon the safe-harbor for forward-looking statements and any such statements made by or on behalf of us are qualified by reference to the following cautionary statements, as well as to those set forth elsewhere in this Form 10-K.*

### RISKS RELATED TO OUR BUSINESS, INDUSTRY AND STRATEGY

**There is uncertainty in the development of our products and if we do not successfully commercialize our products, we will not be profitable.**

In November 2000, we began to market our first product, Argatroban, through our agreement with GSK. However, the royalties produced to date by Argatroban have not made us profitable. To date, the majority of our resources have been dedicated to the research and development of Argatroban and other small molecule drugs for certain vascular and related inflammatory diseases. The commercial applications of our product candidates will require further investment, research, development, preclinical and clinical testing and regulatory approvals, both foreign and domestic. We cannot assure you that we will be able to develop, produce at reasonable cost, or market successfully, any of our product candidates. Further, these product candidates may require complex delivery systems that may prevent or limit their commercial use. All of our products will require regulatory approval before they may be commercialized. Products, if any, resulting from our research and development programs other than Argatroban, are not expected to be commercially available for a number of years, and we cannot assure you that any successfully developed products will generate substantial revenues or that we will ever be profitable.

**We face substantial competition that may result in others developing and commercializing products more successfully than we do.**

The biopharmaceutical industry is highly competitive. Our success will depend on our ability to develop products and apply technology and to establish and maintain a market for our products. Potential competitors in the U.S. and other countries include major pharmaceutical and chemical companies, specialized biotechnology firms, universities and other research institutions. Many of our competitors have substantially greater research and development capabilities and experience and greater manufacturing, marketing and financial resources than we do. Accordingly, our competitors may develop products or other novel technologies that are more effective, safer or less costly than any that have been or are being developed by us or may obtain FDA approval for products more rapidly than we are able.

We expect significant competition for Argatroban for the treatment of HIT. The products that compete with Argatroban include:

- Refludan<sup>®</sup>, which was approved by the FDA in 1997 for the treatment of HIT;
- Orgaran<sup>®</sup>, which is a low molecular weight heparinoid that has been approved for the treatment of deep vein thrombosis, but is believed to be used without an approved indication ("off-label") for the treatment of HIT in the U.S.; and
- Angiomax<sup>®</sup>, which is approved for use in the U.S. as an anticoagulant in patients with unstable angina undergoing percutaneous transluminal coronary angioplasty.

We may also face competition for Argatroban in indications other than HIT, when and if such indications are approved by the FDA, including:

- Revasc<sup>®</sup>, which is used in the treatment of deep vein thrombosis following hip surgery and has received regulatory approval in Europe;

- Angiomax<sup>®</sup>, which is in Phase III clinical trials for acute coronary syndromes and conducting clinical trials in HIT patients;
- Arixtra<sup>®</sup>, which is approved for the prevention of deep vein thrombosis and pulmonary embolism; and
- Melagatran, which is being developed as a treatment for deep vein thrombosis and is in Phase III trials.

We cannot assure you that technological development by others will not render our products or product candidates uncompetitive or that we will be successful in establishing or maintaining technological competitiveness.

**We are dependent on third parties to fund, market and develop our products, including Argatroban.**

We rely on strategic relationships with our corporate partners to provide the financing, marketing and technical support and, in certain cases, the technology necessary to develop and commercialize certain of our product candidates. We have entered into an agreement with Mitsubishi to license rights and technology relating to Argatroban in the U.S. and Canada for specified therapeutic indications. Either party may terminate the Mitsubishi agreement on 60 days notice if the other party defaults in its material obligations under the agreement, declares bankruptcy or becomes insolvent, or if a substantial portion of its property is subject to levy. Unless terminated sooner due to the above-described termination provisions, the agreement with Mitsubishi expires on the later of the termination of patent rights in a particular country or 20 years after the first commercial sale of products in a particular country.

We also entered into an agreement with GSK in 1997 whereby we granted an exclusive sublicense to GSK relating to the continued development and commercialization of Argatroban. This agreement provides for the payment of royalties and certain milestone payments upon the completion of various regulatory filings and receipt of regulatory approvals. The agreement generally terminates on a country-by-country basis upon the earlier of the termination of our rights under the agreement with Mitsubishi, the expiration of applicable patent rights, or in the case of certain royalty payments, the introduction of a substantial competitor for Argatroban by another pharmaceutical company. GSK also has the right to terminate the agreement on a country by country basis by giving us at least three months written notice based on a reasonable determination by GSK that the commercial profile of the therapeutic indication in question would not justify continued development or marketing in that country. In addition, either we or GSK may terminate our agreement on 60 days notice if the other party defaults in its obligations under the agreement, declares bankruptcy or becomes insolvent.

ICOS-TBC has the responsibility for developing endothelin antagonist compounds from our research program. Should the partners not be able to successfully conduct the research and clinical development of the compounds, we could be adversely affected. There is no guarantee that the partnership will have adequate funds to pursue its research and clinical goals or that the effort will be successful. In January 2003, ICOS announced that they had reached a conclusion that joint development of the endothelin receptor antagonist program, through ICOS-TBC should not continue. ICOS and we are currently negotiating the terms pursuant to which we could independently continue the program. We are entirely responsible for independently funding future development activities of ICOS-TBC subsequent to 2002 which we believe will be between \$19 and \$21 million in 2003. A delay in reaching an agreement with ICOS could adversely affect or delay the development of the endothelin receptor antagonist program.

In 2002, the stockholders of Revotar executed an agreement to provide approximately \$4.5 million in unsecured loans, of which our commitment was approximately \$3.4 million. Under the loan agreement, we have advanced approximately \$1.2 million to Revotar during 2002. We believe that Revotar's existing funds, the remaining commitments under the loan agreement and proceeds under German government scientific grants will be sufficient to fund Revotar into the first quarter of 2004. In order to continue to operate beyond that time, Revotar will need to seek additional funding through collaborative arrangements and/or through public or private financings in the future.

Our collaboration and license agreement with Schering-Plough for VLA-4 antagonists contains a provision that allows for termination of the research program upon one hundred eighty days written notice to us.

Our success will depend on these and any future strategic alliances. There can be no assurance that we will satisfy the conditions required to obtain additional research or milestone payments under the existing agreements or that we can prevent the termination of these agreements. We cannot assure you that we will be able to enter into

future strategic alliances on acceptable terms. The termination of any existing strategic alliances or the inability to establish additional collaborative arrangements may limit our ability to develop our technology and may have a material adverse effect on our business or financial condition.

## **RISKS RELATING TO CLINICAL AND REGULATORY MATTERS**

**The regulatory approval process is costly and lengthy and we may not be able to successfully obtain all required regulatory approvals.**

The preclinical development, clinical trials, manufacturing, marketing and labeling of pharmaceuticals are all subject to extensive regulation by numerous governmental authorities and agencies in the U.S. and other countries. We must obtain regulatory approval for each of our product candidates before marketing or selling any of them. It is not possible to predict how long the approval processes of the FDA or any other applicable federal, state or foreign regulatory authority or agency for any of our products will take or whether any such approvals ultimately will be granted. Positive results in preclinical testing and/or early phases of clinical studies offer no assurance of success in later phases of the approval process. Generally, preclinical and clinical testing of products can take many years, and require the expenditure of substantial resources, and the data obtained from these tests and trials can be susceptible to varying interpretation that could delay, limit or prevent regulatory approval. Any delay in obtaining, or failure to obtain, approvals could adversely affect the marketing of our products and our ability to generate product revenue.

The risks associated with the approval process include:

- delays or rejections in the regulatory approval process based on the failure of clinical or other data to meet expectations, or the failure of the product to meet a regulatory agency's requirements for safety, efficacy and quality; and
- regulatory approval, if obtained, may significantly limit the indicated uses for which a product may be marketed.

**Our clinical trials could take longer to complete and cost more than we expect, which may result in our development plans being significantly delayed.**

We will need to conduct clinical studies of all of our product candidates. These studies are costly, time consuming and unpredictable. Any unanticipated costs or delays in our clinical studies could cause us to expend substantial additional funds or to delay or modify our plans significantly, which would harm our business, financial condition and results of operations. The factors that could contribute to such cost, delays or modifications include:

- the cost of conducting human clinical trials for any potential product. These costs can vary dramatically based on a number of factors, including the order and timing of clinical indications pursued and the development and financial support from corporate partners; and
- intense competition in the pharmaceutical market, which may make it difficult for us to obtain sufficient patient populations or clinician support to conduct our clinical trials as planned.

**Even if we obtain marketing approval, our products will be subject to ongoing regulatory oversight, which may affect the success of our products.**

Any regulatory approvals that we receive for a product may be subject to limitations on the indicated uses for which the product may be marketed or contain requirements for potentially costly post-marketing follow-up Phase IV studies. After we obtain marketing approval for any product, the manufacturer and the manufacturing facilities for that product will be subject to continual review and periodic inspections by the FDA and other regulatory authorities. The subsequent discovery of previously unknown problems with the product or with the manufacturer or facility may result in restrictions on the product or manufacturer, including withdrawal of the product from the market.

If we fail to comply with applicable regulatory requirements, we may be subject to fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

## **RISKS RELATING TO FINANCING OUR BUSINESS**

**We have a history of operating losses and an accumulated deficit, and we may not be successful in raising additional funds in the future.**

We have been unprofitable to date and expect to incur operating losses for the next several years as we invest in product research and development, preclinical and clinical testing and regulatory compliance. We will require substantial additional funding to complete the research and development of our product candidates, to establish commercial scale manufacturing facilities, if necessary, and to market our products. We have accumulated approximately \$148.2 million in net losses through December 31, 2002. Estimates of our future capital requirements will depend on many factors, including:

- market acceptance and commercial success of Argatroban;
- expenses and risks associated with clinical trials to expand the indications for Argatroban;
- continued scientific progress in our drug discovery programs;
- the magnitude of these programs;
- progress with preclinical testing and clinical trials;
- the time and costs involved in obtaining regulatory approvals;
- the costs involved in filing, prosecuting and enforcing patent claims;
- competing technological and market developments and changes in our existing research relationships;
- our ability to maintain and establish additional collaborative arrangements; and
- effective commercialization activities and arrangements.

Subject to these factors, we anticipate that our existing capital resources and other revenue sources, should be sufficient to fund our cash requirements through 2004. Notwithstanding revenues, which may be produced through sales of potential future products if approved, we anticipate that we will need to secure additional funds to continue the required levels of research and development to reach our long-term goals. We intend to seek such additional funding through collaborative arrangements and/or through public or private financings.

We cannot assure you that additional financing will be available or, if available, that it will be available on acceptable terms. If additional funds are raised by issuing securities, further dilution of the equity ownership of existing stockholders will result. If adequate funds are not available, we may be required to delay, scale back or eliminate one or more of our drug discovery or development programs or obtain funds through arrangements with collaborative partners or others that may require us to relinquish rights to certain of our technologies, product candidates or products that we would not otherwise relinquish.

**We may experience significant fluctuations in our operating results.**

We have historically experienced, and expect to continue to experience for the foreseeable future, significant fluctuations in our operating results. These fluctuations are due to a number of factors, many of which are outside of our control, and may result in volatility of our stock price. Future operating results will depend on many factors, including:

- demand for our products;
- regulatory approvals for our products;

- the timing of the introduction and market acceptance of new products by us or competing companies; and
- the timing and magnitude of certain research and development expenses.

## **RISKS RELATED TO ONGOING OPERATIONS**

### **We are dependent on qualified personnel.**

Our success is highly dependent on our ability to attract and retain qualified scientific and management personnel. The loss of the services of the principal members of our management and scientific staff including Bruce D. Given, M.D., our President and Chief Executive Officer, and Richard A.F. Dixon, Ph.D., our Senior Vice President, Research and Chief Scientific Officer, may impede our ability to bring products to market. In order to commercialize products, we must maintain and expand our personnel as needs arise in the areas of research, clinical trial management, manufacturing, sales and marketing. We face intense competition for such personnel from other companies, academic institutions, government entities and other organizations. We cannot assure you that we will be successful in hiring or retaining qualified personnel. Managing the integration of new personnel and our growth in general could pose significant risks to our development and progress.

We also rely on consultants and advisors to assist us in formulating our research and development strategy. All our consultants and advisors are either self-employed or employed by other organizations, and they may have other commitments such as consulting or advisory contracts with other organizations that may affect their ability to contribute to us.

### **The hazardous material we use in our research and development could result in significant liabilities, which may exceed our insurance coverage.**

Our research and development activities involve the use of hazardous materials. While we believe that we are currently in substantial compliance with federal, state and local laws and regulations governing the use of these materials, accidental injury or contamination may occur. Any such accident or contamination could result in substantial liabilities, which could exceed the policy limits of our insurance coverage and financial resources. Additionally, the cost of compliance with environmental and safety laws and regulations may increase in the future.

### **We may be sued for product liability, which may prevent or interfere with the development or commercialization of our products.**

Because our products and product candidates are new treatments, with limited, if any, past use on humans, serious undesirable and unintended side effects may arise. We may be subject to product liability claims that are inherent in the testing, manufacturing, marketing and sale of pharmaceutical products. These claims could expose us to significant liabilities that could prevent or interfere with the development or commercialization of our products and seriously impair our financial position. Product liability insurance is generally expensive for biopharmaceutical companies such as ours. We maintain product liability insurance coverage for claims arising from the use of our products in clinical trials prior to FDA approval. Under the agreements with Mitsubishi and GSK, we maintain product liability insurance to cover claims that may arise from the sale of Argatroban. Our existing coverage will not be adequate as we further develop products and continue to sell Argatroban. We cannot assure you that we will be able to maintain our existing insurance coverage or obtain additional coverage on commercially reasonable terms for liability arising from the use of our other products in the future. Also, this insurance coverage and our resources may not be sufficient to satisfy any liability resulting from product liability claims and a product liability claim may have a material adverse effect on our business, financial condition or results of operations.

## **RISKS RELATING TO PRODUCT MANUFACTURING AND SALES**

### **We have very limited manufacturing, marketing or sales experience.**

We have very limited manufacturing, marketing or product sales experience. If we develop any additional commercially marketable products, we cannot assure you that contract manufacturing services will be available in sufficient capacity to supply our product needs on a timely basis. If we decide to build or acquire commercial scale manufacturing capabilities, we will require additional management and technical personnel and additional capital.

If in the future, we decide to perform sales and marketing activities ourselves, we would face a number of additional risks, including:

- we may not be able to attract and build a significant marketing or sales force;
- the cost of establishing a marketing or sales force may not be justifiable in light of product revenues; and
- our direct sales and marketing efforts may not be successful.

**We cannot assure you that the raw materials necessary for the manufacture of our products will be available in sufficient quantities or at a reasonable cost.**

Complications or delays in obtaining raw materials or in product manufacturing could delay the submission of products for regulatory approval and the initiation of new development programs, each of which could materially impair our competitive position and potential profitability. We can give no assurance that we will be able to enter into any other supply arrangements on acceptable terms, if at all.

**We are dependent on a single supplier of Argatroban.**

At the present time, Mitsubishi is the only manufacturer of Argatroban in bulk form. Mitsubishi has entered into a supply agreement with GSK to supply Argatroban in bulk to meet GSK's and our needs. Should Mitsubishi fail during any consecutive nine-month period to supply GSK with at least 80 percent of its requirements, and such requirements cannot be satisfied by existing inventories, the supply agreement with Mitsubishi provides for the nonexclusive transfer of the production technology to GSK. However, in the event Mitsubishi terminates manufacturing Argatroban or defaults in its supply commitment, we cannot assure you that GSK will be able to commence manufacturing of Argatroban in a timely manner or that alternate sources of bulk Argatroban will be available at reasonable cost, if at all. If GSK cannot commence the manufacturing of Argatroban or alternate sources of supply are unavailable or are not available on commercially reasonable terms, it could harm our profitability. In addition, finishing and packaging has only been arranged with one manufacturing facility in the U.S. GSK has informed us that they will be finishing and packaging in a GSK facility sometime in the future.

**Our products, even if approved by the FDA or foreign regulatory agencies, may not be accepted by health care providers, insurers or patients.**

If any of our products, including Argatroban, after receiving FDA or other foreign regulatory approval, fail to achieve market acceptance, our ability to become profitable in the future will be adversely affected. We believe that market acceptance will depend on our ability to provide acceptable evidence of safety, efficacy and cost effectiveness. In addition, market acceptance depends on the effectiveness of our marketing strategy and the availability of reimbursement for our products.

**The successful commercialization of our products is dependent on pharmaceutical pricing and third-party reimbursement.**

In recent years, there have been numerous proposals to change the health care system in the United States. Some of these proposals have included measures that would limit or eliminate payments for medical procedures and treatments or subject the pricing of pharmaceuticals to government control. In addition, government and private third-party payors are increasingly attempting to contain health care costs by limiting both the coverage and the level of reimbursement of drug products. Consequently, the reimbursement status of newly approved health care products is highly uncertain, and there can be no assurance that third-party coverage will be available or that available third-party coverage will enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. Our long-term ability to market products successfully may depend in part on the extent to which reimbursement for the cost of such products and related treatment will be available. Third-party payors are increasingly challenging the prices of medical products and services. Furthermore, inadequate third-party coverage may reduce market acceptance of our products. Significant changes in the health care system in the United States or elsewhere could have a material adverse effect on our business and financial performance.

Sitaxsentan is likely to require distribution through a limited access program which may make patient access and reimbursement more difficult. Tracleer<sup>®</sup> is distributed pursuant to such a program.

## **RISKS RELATING TO INTELLECTUAL PROPERTY**

### **We may not be able to protect proprietary information and obtain patent protection.**

We actively seek patent protection for our proprietary technology, both in the U.S. and in other areas of the world. However, the patent positions of pharmaceutical and biotechnology companies, including us, are generally uncertain and involve complex legal, scientific and factual issues. Intellectual property is an uncertain and developing area of the law that is potentially subject to significant change. Our success will depend significantly on our ability to:

- obtain patents;
- protect trade secrets;
- operate without infringing upon the proprietary rights of others; and
- prevent others from infringing on our proprietary rights.

We cannot assure you that patents issued to or licensed by us will not be challenged, invalidated or circumvented, or that the rights granted will provide competitive advantages to us. We cannot assure you that our patent applications or pending patent applications, if and when issued, will be valid and enforceable and withstand litigation. We cannot assure you that others will not independently develop substantially equivalent, generic equivalent or superseding proprietary technology or that an equivalent product will not be marketed in competition with our products, thereby substantially reducing the value of our proprietary rights. We may experience a significant delay in obtaining patent protection for our products as a result of a substantial backlog of pharmaceutical and biotechnology patent applications at the PTO. Because patent applications in the U.S. are maintained in secrecy until patents issue, other competitors may have filed or maintained patent applications for technology used by us or covered by pending applications without our being aware of these applications. In addition, patent protection, even if obtained, is affected by the limited period of time for which a patent is effective. The Mitsubishi composition of matter patent on Argatroban has expired. Moreover, even if we have a patent or NDA exclusivity, we cannot assure you that generic pharmaceutical manufacturers will not ultimately enter the market and compete with us or that competitors might develop a different formulation of Argatroban.

We could also incur substantial costs in defending any patent infringement suits or in asserting any patent rights, including those granted by third parties, in a suit with another party. The PTO could institute interference proceedings involving us in connection with one or more of our patents or patent applications, and such proceedings could result in an adverse decision as to priority of invention. The PTO or a comparable agency in a foreign jurisdiction could also institute re-examination or opposition proceedings against us in connection with one or more of our patents or patent applications and such proceedings could result in an adverse decision as to the validity or scope of the patents.

We may be required to obtain licenses to patents or other proprietary rights from third parties. We cannot assure you that any licenses required under any patents or proprietary rights would be made available on acceptable terms, if at all. If we are unable to obtain required licenses, we could encounter delays in product introductions while we attempt to design around blocking patents, or we could find that the development, manufacture or sale of products requiring such licenses could be foreclosed.

### **If we are unable to keep our trade secrets confidential, our technology and information may be used by others to compete against us.**

We rely significantly on trade secrets, know-how and continuing technological advancement to maintain our competitive position. We try to protect this information by entering into confidentiality agreements with our employees and consultants, which contain assignment of invention provisions. Notwithstanding these agreements, others may gain access to these trade secrets, such agreements may not be honored and we may not be able to protect effectively our rights to our unpatented trade secrets. Moreover, our trade secrets may otherwise become known or independently developed by our competitors.

## RISKS RELATED TO OUR COMMON STOCK OUTSTANDING

### **Our stock price could be volatile.**

The stock market has from time to time experienced significant price and volume fluctuations that may be unrelated to the operating performance of particular companies. In particular, the market price of our common stock, like that of the securities of other biopharmaceutical companies, has been and may be highly volatile. Factors such as announcements concerning technological innovations, new commercial products or procedures by us or our competitors, proposed governmental regulations and developments in both the U.S. and foreign countries, disputes relating to patents or proprietary rights, publicity regarding actual or potential medical results relating to products under development by us or our competitors, public concern as to the safety of biotechnology products, and economic and other external factors, as well as period-to-period fluctuations and financial results, may have a significant effect on the market price of our common stock.

From time to time, there has been limited trading volume with respect to our common stock. In addition, there can be no assurance that there will continue to be a trading market or that any securities research analysts will continue to provide research coverage with respect to our common stock. It is possible that such factors will adversely affect the market for our common stock.

On March 21, 2003, Nasdaq informed us that for the last 30 consecutive trading days, the bid price of our common stock has closed below the minimum \$1.00 per share requirement for continued inclusion in The Nasdaq National Market. Therefore, in accordance with Nasdaq Rules, we will be provided 180 calendar days, or until September 17, 2003, to regain compliance. If, at any time before September 17, 2003, the bid price of our common stock closes at \$1.00 per share or more for a minimum of 10 consecutive trading days, the Nasdaq will provide written notification that we have achieved compliance with this rule. If compliance with this rule cannot be demonstrated by September 17, 2003, the Nasdaq will provide written notification that our securities will be delisted. At that time, we may appeal this determination to a Listing Qualifications Panel or may apply to transfer our securities to The Nasdaq Small Cap Market.

### **The number of shares of our common stock eligible for future sale, including warrants, which are currently exercisable, could adversely affect the market price of our stock.**

As of December 31, 2002, we have reserved approximately 6.0 million shares of common stock for issuance under outstanding options, warrants and other contingent agreements. Approximately 5.8 million of these shares of common stock are registered for sale or resale on currently effective registration statements, and the holders of substantially all of the remaining shares of common stock are entitled to registration rights. The issuance of a significant number of shares of common stock upon the exercise of stock options and warrants, or the sale of a substantial number of shares of common stock under Rule 144 or otherwise, could adversely affect the market price of the common stock.

### **Certain anti-takeover provisions in our certificate of incorporation and Delaware law may deter or prevent a change in control of our company, even if that change would be beneficial to our stockholders.**

Our Certificate of Incorporation and the provisions of Section 203 of the Delaware General Corporation Law contain certain provisions that may delay or prevent an attempt by a third party to acquire control of us. Additionally, we adopted a Shareholder Rights Plan in January 2002 that may delay or prevent such attempt by a third party to acquire control of us. In addition, the severance provisions of employment agreements with certain members of management could impede an attempted change of control by a third party.

## **ITEM 2 — PROPERTIES**

We lease 15,490 square feet of office space in Bellaire, Texas for our administrative, marketing, clinical development and regulatory departments. The lease expires July 31, 2005 with an option to extend the lease to December 31, 2005, provided we give ninety (90) days prior written notice.

We also lease 31,359 square feet of office and laboratory space in another building in Houston, Texas for our research department, including a 21,621 square foot laboratory facility and a 3,909 square foot animal facility. The



remaining area is being used for clinical development, computer modeling, storage space and additional offices for scientists. Our lease expires in December 2005. Additionally, we lease 658 square feet in the building for use as storage space on a monthly basis.

Revotar leases 8,800 square feet of office and laboratory space in Berlin, Germany. Their lease expires in September 2006.

We may require additional space to accommodate future research and laboratory needs as necessary to bring products into development and clinical trials.

**ITEM 3 — LEGAL PROCEEDINGS**

None

**ITEM 4 — SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS**

No matters were submitted to a vote of our shareholders during the fourth quarter of our fiscal year ended December 31, 2002.

**PART II**

**ITEM 5 — MARKET FOR THE REGISTRANT'S COMMON EQUITY AND RELATED STOCKHOLDER MATTERS**

Our common stock began trading on The Nasdaq National Market on June 19, 2001 under the symbol "TXBI" before which our common stock was traded on the American Stock Exchange under the symbol "TXB".

On March 21, 2003, Nasdaq informed us that for the last 30 consecutive trading days, the bid price of our common stock has closed below the minimum \$1.00 per share requirement for continued inclusion in The Nasdaq National Market. Therefore, in accordance with Nasdaq Rules, we will be provided 180 calendar days, or until September 17, 2003, to regain compliance. If, at any time before September 17, 2003, the bid price of our common stock closes at \$1.00 per share or more for a minimum of 10 consecutive trading days, Nasdaq will provide written notification that we have achieved compliance with this rule. If compliance with this rule cannot be demonstrated by September 17, 2003, the Nasdaq will provide written notification that our securities will be delisted. At that time, we may appeal this determination to a Listing Qualifications Panel or may apply to transfer our securities to The Nasdaq Small Cap Market.

The following table sets forth, for the periods indicated, the high and low sale prices for the common stock as reported by the consolidated transaction reporting system.

	<u>Common Stock</u>	
	<u>High</u>	<u>Low</u>
<b>Year ended December 31, 2001</b>		
First Quarter .....	10.90	4.62
Second Quarter .....	9.00	4.51
Third Quarter .....	8.60	4.90
Fourth Quarter .....	7.47	5.02
<b>Year ended December 31, 2002</b>		
First Quarter .....	7.10	5.03
Second Quarter .....	6.10	2.94
Third Quarter .....	3.71	1.80
Fourth Quarter .....	3.08	1.30

As of March 15, 2003 there were approximately 476 holders of record of our common stock and approximately 16,000 beneficial owners.

**EQUITY COMPENSATION PLAN INFORMATION**

<u>Plan Category</u>	<u>(a) Number of securities to be issued upon exercise of outstanding options, warrants and rights</u>	<u>Weighted-average exercise price of outstanding options, warrants and rights</u>	<u>Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in Column (a))</u>
Equity compensation plans approved by security holders	5,012,500	\$6.72	745,913
Equity compensation plans not approved by security holders	---	---	---
<b>Total</b>	<u>5,012,500</u>	<u>\$6.72</u>	<u>745,913</u>

See Note 3 to the Consolidated Financial Statements, included herein.

## **DIVIDEND POLICY**

We have never declared or paid dividends on our common stock. We do not anticipate paying any cash dividends in the foreseeable future. We intend to retain any future earnings to finance our growth strategy and ongoing business. Payment of future dividends, if any, will be at the discretion of the board of directors after reviewing various factors, including our financial condition and operating results, current and anticipated cash needs and restrictions which may be in effect in any future financing agreement.

## **RECENT SALES OF UNREGISTERED SECURITIES**

None.

**ITEM 6 — SELECTED FINANCIAL DATA**  
*(In thousands, except per share amounts)*

The selected financial data set forth below for each of the years in the five-year period ended December 31, 2002 are derived from our audited consolidated financial statements. The selected financial data set forth below should be read in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our 2002, 2001 and 2000 financial statements and notes thereto included elsewhere in this Form 10-K.

	<u>Year Ended December 31,</u>				
	<u>2002</u>	<u>2001</u>	<u>2000</u>	<u>1999</u>	<u>1998</u>
<b>Consolidated Statement of Operations</b>					
<b>Data:</b>					
Revenues.....	\$ 10,433	\$ 8,917	\$ 15,692	\$ 2,083	\$ 2,252
Expenses:					
Research and development.....	20,066	17,861	13,513	13,080	14,399
Equity in loss of affiliate.....	8,557	9,450	3,487	---	---
Charge for purchase of in-process research and development.....	---	---	---	---	134
General and administrative.....	<u>8,976</u>	<u>6,733</u>	<u>6,552</u>	<u>5,512</u>	<u>4,321</u>
Total expenses.....	<u>37,599</u>	<u>34,044</u>	<u>23,552</u>	<u>18,592</u>	<u>18,854</u>
Operating loss.....	(27,166)	(25,127)	(7,860)	(16,509)	(16,602)
Investment income, net.....	<u>2,472</u>	<u>5,236</u>	<u>4,362</u>	<u>1,212</u>	<u>2,088</u>
Loss before minority interest and cumulative effect of change in accounting principle.....	(24,694)	(19,891)	(3,498)	(15,297)	(14,514)
Minority interest in loss of Revotar.....	<u>1,225</u>	<u>749</u>	<u>209</u>	---	---
Loss before cumulative effect of change in accounting principle.....	(23,469)	(19,142)	(3,289)	(15,297)	(14,514)
Cumulative effect of change in accounting principle.....	---	---	<u>(2,366)</u>	---	---
Net loss.....	(23,469)	(19,142)	(5,655)	(15,297)	(14,514)
Preferred dividend requirement.....	---	---	---	---	(2)
Net loss applicable to common shares.....	<u>\$(23,469)</u>	<u>\$(19,142)</u>	<u>\$(5,655)</u>	<u>\$(15,297)</u>	<u>\$(14,516)</u>
Net loss per share basic and diluted.....	<u>\$(0.54)</u>	<u>\$(0.44)</u>	<u>\$(0.14)</u>	<u>\$(0.45)</u>	<u>\$(0.43)</u>
Weighted average common shares used to compute basic and diluted net loss per share.....	<u>43,741</u>	<u>43,637</u>	<u>39,150</u>	<u>34,226</u>	<u>33,930</u>
	<u>December 31,</u>				
	<u>2002</u>	<u>2001</u>	<u>2000</u>	<u>1999</u>	<u>1998</u>
<b>Consolidated Balance Sheet Data:</b>					
Cash, cash equivalents and short and long-term investments.....	\$ 68,005	\$ 95,427	\$ 92,533	\$ 15,170	\$ 30,376
Working capital.....	44,965	52,322	85,041	14,477	27,907
Total assets.....	77,792	104,362	98,969	20,805	36,106
Shareholders' equity.....	62,078	84,237	84,027	18,590	33,236

## **ITEM 7 — MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS**

The following discussion of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and the related notes to the financial statements included elsewhere in this Form 10-K. This discussion contains forward-looking statements based on current expectations that are subject to risks and uncertainties, such as statements of our plans, objectives, expectations and intentions. When used in this discussion, the words "expect", "anticipate", "intend", "plan", "believe", "seek", "estimate" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Our actual results and the timing of events could differ materially from those anticipated or implied by the forward-looking statements discussed here as a result of various factors, including, among others, those set forth under the "Cautionary Note Regarding Forward-Looking Statements", herein. You should not place undue reliance on these forward-looking statements, which speak only as of the date of this report. Except as required by law, we undertake no obligation to update any of the forward-looking statements in this discussion after the date of this report.

### **Overview**

Since our inception in 1989, we have primarily devoted our resources to funding drug discovery, research and development. We are a biopharmaceutical company focused on the discovery, development and commercialization of novel, synthetic, small molecule compounds for the treatment of a variety of cardiovascular, vascular and related inflammatory diseases. Our research and development programs are focused on inhibitors (also referred to as antagonists or blockers) that can interrupt certain disease processes. Our programs seek to address unmet medical needs in areas where our compounds will have the greatest likelihood of improving the lives of patients suffering from cardiovascular diseases, thrombocytopenia, pulmonary arterial hypertension, heart failure and inflammatory diseases such as asthma.

Our strategy is to identify and develop novel product candidates for underserved indications, and to commercialize those candidates through collaborations with other pharmaceutical and biotechnology companies. An important part of our strategy is the selection of corporate partners to enhance our drug discovery and development efforts. We and our partners currently have three products in clinical development.

For additional information about our programs and business strategy, see "Overview" and "Business Strategy" in Item 1, "Business" included herein.

### **Major Compounds in Research and Development Programs**

#### **Argatroban**

Argatroban is our first marketed product. Argatroban was approved by the U.S. FDA in 2000, is indicated for prophylaxis or treatment of thrombosis in patients with HIT for patients with or at risk of HIT undergoing PCI. Argatroban was approved in Canada in 2002 for use as anticoagulant therapy in patients with heparin-induced thrombocytopenia syndrome. The drug is being marketed in the U.S. and Canada by GSK and has been on the market in the U.S. and Canada since November 2000 and June 2002, respectively. GSK is our development, manufacturing and marketing partner for Argatroban.

During 2002, we completed a Phase II human clinical trial for Argatroban as a mono-therapy treatment for acute ischemic stroke. The clinical trial met the primary endpoint and showed positive results in the secondary safety endpoint. In light of a lack of an overall efficacy trend and the high risk and high cost associated with stroke trials, it is unlikely that we will proceed independently with a full Phase II program. Currently, Argatroban is being evaluated by an investigator at the University of Texas Medical School at Houston in a clinical trial, in combination with recombinant tissue Plasminogen Activator ("rt-PA") as a new approach to the treatment of acute ischemic stroke. Argatroban is approved and sold in Japan by Mitsubishi, the licensor of Argatroban and by their licensee as mono-therapy for an indication of acute ischemic stroke.

We, along with GSK, are continuing to evaluate the use of Argatroban for use in hemodialysis patients and for use in PCI.

Presently, we have four major product development programs.

- *Endothelin Antagonist Program.* We are developing sitaxsentan, an endothelin (A) receptor antagonist, or ET<sub>A</sub>, for the treatment of pulmonary arterial hypertension. During June 2000, we formed a partnership, ICOS-TBC, with ICOS Corporation to develop and commercialize ET<sub>A</sub> receptor antagonists. During 2002, ICOS-TBC successfully completed a Phase IIB/III clinical trial in pulmonary arterial hypertension with sitaxsentan. TBC3711, a second generation ET<sub>A</sub>, has previously completed Phase I clinical trials and may be developed for cardiovascular or other diseases. In January 2003, ICOS announced that they had reached a conclusion that joint development of the endothelin receptor antagonist program by ICOS-TBC should not continue. ICOS and TBC are currently negotiating the terms pursuant to which TBC could independently continue the program. The financial terms of this transaction are subject to ongoing negotiations between the two companies. After 2002, we are responsible for all costs of the program.
- *Thrombolysis.* During 2002, we completed a Phase II human clinical trial for Argatroban as a mono-therapy treatment for acute ischemic stroke. The clinical trial met the primary endpoint based on safety and showed positive results in the secondary safety endpoint. In light of a lack of a positive overall efficacy trend and the high risk and high costs associated with stroke trials, it is unlikely that we will proceed independently with a full Phase II program. Currently, Argatroban is being evaluated, in a clinical trial, in combination with recombinant tissue Plasminogen Activator ("rt-PA") as a new approach to the treatment of acute ischemic stroke by an investigator at the University of Texas Medical School at Houston.
- *Vascular Inflammation Program.* Revotar, our majority owned German affiliate located in Berlin is developing a selectin antagonist, bimosiamose, for the treatment of asthma and psoriasis. The intravenous form of the drug demonstrated positive anti-inflammatory effects in Phase II clinical trials. Revotar was formed during 2000, to further the development of this program. Revotar completed Phase I clinical trials for asthma utilizing an inhaled form of bimosiamose. A Phase IIa clinical trial is currently being conducted with an inhaled form of bimosiamose and a Phase IIa clinical trial in psoriasis is planned to commence during the first half of 2003, using a topical formulation. A Phase IIa proof-of-concept clinical trial in psoriasis, completed during 2002 with an injectable form of bimosiamose, demonstrated efficacy. We are also conducting research with respect to other cell adhesion molecules including vascular cell adhesion molecule, or VCAM, junctional adhesion molecules, or JAM 2/3 and several integrins including very late antigen 4, or VLA-4,  $\alpha 4\beta 7$  and others to develop antagonists for the treatment of asthma, rheumatoid arthritis, multiple sclerosis, restenosis and inflammatory bowel disease. We have signed a collaboration and license agreement for the VLA-4 program with Schering-Plough and have received a milestone payment from Schering-Plough for nominating a compound as a clinical candidate. Additionally, we are conducting research on backup VLA-4 antagonists for Schering-Plough under this agreement.
- *Vascular Disease.* Many disease processes involve changes in blood vessels and heart tissue. There are numerous mediators, like endothelin, which may contribute to the development of these diseases. Several of these act through G-protein coupled receptors, GPCRs, to carry out their action. We are conducting research on urotensin and other GPCRs to identify inhibitors which could be useful in treating diseases including congestive heart failure, CHF, ischemic stroke and acute myocardial infarction.

## Results of Operations

### *Critical Accounting Policies*

#### *Revenue Recognition*

- We recognize revenue from service contracts as services are performed.
- Royalty revenue is recognized as products are sold by a licensee and we have received sufficient information to record a receivable. Our royalty revenue is based on net sales of product, that is, sales net of discounts, returns and allowances. We have estimated a percentage of gross sales, based on recent experience, as an allowance for future returns, however there can be no assurance that our estimate will be accurate.

- Revenue from collaborative research and development activities is recognized as services are performed.
- We defer the recognition of milestone payments related to contractual agreements which are still in the development stage. Such deferred revenues are amortized into income over the estimated remaining development period. Milestone payments received under contractual agreements which have completed the development stage are evaluated, and either recognized into income when earned, or amortized over a future period, depending upon whether the Company continues to have obligations under the terms of the arrangement.
- License fees received under the terms of licensing agreements for our intellectual property are deferred, and amortized into income over the estimated development period of the licensed item or items.
- Revenue from grants is recognized as earned under the terms of the related grant agreements, typically as expenses are incurred.

Amounts received in advance of services being performed under contracts are recorded as deferred revenue, and recognized as services are performed. We periodically evaluate our estimates of remaining development periods, and adjust the recognition of remaining deferred revenues over the adjusted development period remaining.

#### *Partnership Accounting*

We recognize our share of the operating results of ICOS-TBC in proportion to our ownership interest and record it as equity in loss of ICOS-TBC. Operating results of ICOS-TBC include reimbursed expenses related to our internal research staff that we recognize as revenue and record as collaborative research and development revenue from ICOS-TBC. Due to the nature of the ICOS-TBC collaborative agreement, our collaborative research and development revenue from ICOS-TBC largely depends on the continued progression of clinical trial and development activities, and can be expected to vary from quarter to quarter and year to year.

In January 2003, ICOS informed us that they had reached the conclusion that joint development of the endothelin receptor antagonist program through ICOS-TBC should not continue. ICOS and TBC are currently negotiating the terms pursuant to which we could independently continue the program. The financial terms of this transaction are subject to ongoing negotiations between the two companies. This could allow us to increase our ownership and the potential commercial benefit of the program from 50% to 100%. The partners were responsible for the equal funding of the costs of research and development incurred through the end of 2002. After 2002, we are responsible for all costs of the program.

#### *Stock Options*

We apply Accounting Principles Board Opinion No. 25, "Accounting for Stock Issued to Employees", and related interpretations ("APB 25") in accounting for our stock option plans and apply Financial Accounting Standards Board ("FASB") Statement No. 123, "Accounting for Stock-Based Compensation"; and related interpretations ("SFAS 123") in reporting for our stock option plans. APB 25 utilizes the "intrinsic value" of stock options, defined as the difference between the exercise price of an option and the market price of the underlying share of common stock, on the "measurement date" which is generally the date of grant. Since the exercise price of employee stock options issued under our plans is set to match the market price of our common stock, there is generally no compensation expense recognized upon grant of employee stock options. Options granted to non-employees, if any, are valued at the "fair value" of the option as defined by SFAS 123, utilizing the Black-Scholes option pricing model. We record compensation expense for the "fair value" of options granted to non-employees.

#### *Use of Estimates*

The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities, disclosures of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period.

## General

Our operating results have fluctuated significantly during each quarter and year, and we anticipate that such fluctuations, which are largely attributable to varying research and development commitments and expenditures, will continue for the next several years.

We have been unprofitable to date and expect to incur substantial operating losses for the next several years as we invest in product research and development, preclinical and clinical testing and regulatory compliance. We have sustained net losses of approximately \$148.2 million from the date of our inception to December 31, 2002. We have primarily financed our operations to date through a series of private placements and public offerings of our common stock and several collaborative agreements with third parties to jointly pursue product research and development. See discussion of "Liquidity and Capital Resources" below. See also "Additional Risk Factors" in Item 1 "Business" herein.

### *Year ended December 31, 2002 Compared with Year ended December 31, 2001*

Revenues in the year ended December 31, 2002 increased \$1,516,000, compared with the year ended December 31, 2001. The increase is primarily attributable to increased royalty income earned on sales of Argatroban by GSK and increased license fees, milestones and grants, partially offset by reduced research and development revenues, discussed below.

Royalties earned on sales of Argatroban in 2002 were \$3,514,000, an increase of \$1,928,000 over year 2001. We earn royalties based upon sales by GSK to drug wholesalers. In October 2002, GSK initiated a broad-based HIT disease education media campaign designed to increase awareness of HIT, the life-threatening reaction to heparin for which Argatroban is approved. As medical education is key to growing Argatroban sales, we believe this initiative, along with increased selling efforts, are likely to have a positive impact on Argatroban sales.

License fees, milestones and grants increased \$712,000 in 2002, compared with 2001. Revotar has been awarded research grants from the German government and earned approximately \$303,000 in year 2002. In addition to the grants received by Revotar, the increase in license fees, milestones and grants in 2002 was primarily comprised of revenues related to the milestone payment received from Mitsubishi in May 2001, the milestone payment received from ICOS in July 2001, and the milestone payment received from Schering-Plough in June 2002. See Note 8 to the Consolidated Financial Statements.

Research agreement revenues, resulting from the Company's collaborative efforts with unrelated parties, declined \$772,000 in 2002, compared with 2001, primarily resulting from reduced research and development effort under the Schering-Plough agreement during 2002. Most of our efforts toward development of an initial candidate for clinical development had been completed late in 2001. As discussed above, we received a milestone payment under the Schering-Plough agreement as a result of the nomination of an initial candidate for Schering-Plough's further development in the second quarter of 2002.

Collaborative research and development revenues received from the ICOS-TBC partnership declined \$352,000 in 2002, compared with 2001. The involvement of our research and development staff in the endothelin receptor antagonist program has been dependent upon the activities being performed by the partnership in any particular period, and was expected to fluctuate from quarter to quarter and year to year. In January 2003, ICOS announced that it had reached a conclusion that joint development of the endothelin receptor antagonist program by ICOS-TBC should not continue. ICOS and TBC are currently negotiating the terms pursuant to which TBC could independently continue the program. The financial terms of this transaction are subject to ongoing negotiations between the two companies.

Research and development expenses increased \$2,205,000 in 2002, compared with 2001. The increase is primarily due to costs of clinical trials which began to incur significant expenses early in year 2002 and were ongoing during year 2002. Trials ongoing during year 2002 included a Phase II study of Argatroban in ischemic stroke and a Phase II study of Argatroban in patients undergoing PCI. During 2002, Revotar completed a Phase IIa proof-of-concept clinical trial of bimosiamose in psoriasis, and completed a Phase I clinical trial for asthma utilizing an inhaled form of bimosiamose. See also the discussion of our ongoing research and development programs, above.



Our equity in the loss of the ICOS-TBC partnership, primarily consisting of research and development expenses, declined \$893,000 in 2002, compared with 2001. The principle activity of the partnership, a Phase IIB/III trial of sitaxsentan for PAH, completed enrollment in July 2002.

General and administrative expenses increased \$2,243,000 in 2002, compared with 2001. Insurance costs, particularly product liability and general liability policies, increased both due to insurance market conditions, and as a result of increased sales of Argatroban. General and administrative expenses in 2002 included costs associated with the retirement, recruiting and hiring of key personnel, including a non-cash charge in the first quarter of 2002 of approximately \$182,000 in compensation expense arising from modifications made to stock options previously issued to our retiring CEO.

Investment income declined \$2,764,000 in 2002, compared with 2001. The decline is due to a combination of lower prevailing interest rates during 2002, compared with 2001, and to reduced funds available for investment during year 2002.

The interest of Revotar's minority shareholders in its losses increased approximately \$476,000 in 2002, compared with 2001. Revotar's expenses increased in 2002, primarily due to the costs of clinical trials conducted in 2002. Under accounting principles generally accepted in the U.S., it is likely that the cumulative losses of Revotar will exceed the equity interest of its minority shareholders during 2004, and we will reflect 100% of its losses in our consolidated net income or loss thereafter.

Our net loss in 2002 increased \$4,327,000 in 2002, compared with 2001. The increase is due primarily to higher operating expenses and lower investment income during 2002, as discussed above.

*Year ended December 31, 2001 Compared with Year ended December 31, 2000*

Revenues in the year ended December 31, 2001 decreased \$6,775,000, compared with the year ended December 31, 2000. License fee and milestone income in year 2000 included a milestone payment of \$7,500,000 from GSK which was earned upon the approval of Argatroban by the FDA in June 2000, and the recognition of \$2,366,000 in remaining unrecognized license fees and milestones related to Argatroban. After taking the \$9,866,000 in revenues related to Argatroban into consideration, revenues from other license fees and milestones increased \$967,000, as a result of the recognition of a portion of the license fees and milestones received from Schering-Plough, Mitsubishi and ICOS-TBC in 2000 and 2001. See Notes 7 and 8 to the Consolidated Financial Statements, included herein.

Revenues from sources other than license fees and milestones increased \$2,124,000 in 2001, compared with 2000. Royalties earned on the sale of Argatroban, which was first shipped in the fourth quarter of 2000, increased \$1,352,000 in year 2001 compared with year 2000. Research agreement revenues in year 2001 increased \$453,000, which is comprised of payments received from Schering-Plough, partially offset by the loss of revenues received from LG Chemical in 2000, but not in 2001. Research payments from ICOS-TBC increased \$319,000 in year 2001. The partnership was formed in June 2000, however, and as such, the year 2000 only included six months of operations.

Research and development expenses increased \$4,348,000 in year 2001, compared with year 2000. The increase is primarily due to costs associated with ongoing clinical trials. During year 2001, the Company and its research partners initiated two Phase II trials for Argatroban, for ischemic stroke and PCI, and a Phase I study of TBC1269 for asthma.

Our equity in the losses of ICOS-TBC increased \$5,963,000 in year 2001 compared with year 2000. Since the partnership was formed in June 2000, year 2000 results only included six months of operations. The increase, however, is primarily due to clinical trials conducted in year 2001. In 2001, ICOS-TBC initiated a Phase IIB/III clinical trial for sitaxsentan as a treatment of PAH, and two Phase I clinical studies of TBC3711.

General and administrative expense increased \$181,000 in year 2001, compared to year 2000. The increase is primarily due to the expenses of Revotar, which was formed in June of year 2000.

Investment income increased \$874,000 in year 2001, due to higher levels of invested funds in the current year. We received approximately \$20.1 million in proceeds from the exercise of publicly traded warrants in January 2001.

The effect on investment income of higher availability of funds was partially offset, however, by the lower interest rates which have prevailed during year 2001.

The interest of the minority shareholders of Revotar, who collectively hold approximately 45% of the Revotar common stock, increased \$540,000 in year 2001, compared with 2000, due to higher operating expenses of Revotar in 2001. As discussed above, Revotar was formed in June of year 2000.

Loss before cumulative effect of change in accounting principle increased \$15,853,000 in year 2001, compared with year 2000. The increased loss in year 2001 is primarily due to (i) the \$9,866,000 in license fee and milestone revenues related to Argatroban included in year 2000, discussed above, (ii) increased research and development costs of \$4,348,000, discussed above, (iii) increased equity in loss of ICOS-TBC, primarily due to increased development costs, discussed above, and (iv) increased general and administrative costs of \$181,000, primarily due to the expenses of Revotar, as discussed above. Partially offsetting the effect of reduced revenues and increased costs, investment income increased \$874,000 in year 2001, due to higher levels of available funds, as discussed above.

Net loss in year 2000 included a charge of \$2,366,000 for the cumulative effect, on January 1, 2000, of the change in accounting principle resulting from our adoption of Securities and Exchange Commission ("SEC") Staff Accounting Bulletin No. 101, Revenue Recognition in Financial Statements ("SAB101"). Such revenue is being recognized into income over future development periods.

### Liquidity and Capital Resources

#### *Year 2002 and 2001*

At December 31, 2002, we had cash, cash equivalents, investment securities and accrued interest of \$68,005,000, compared with \$95,427,000 at December 31, 2001. We used \$25,791,000 in cash on operating activities in year 2002, compared to cash used by operating activities of \$12,980,000 in 2001. The primary operating uses of cash in 2002 and 2001 were to fund our general operating expenses and the ongoing research and development programs conducted by TBC, Revotar and ICOS-TBC, reduced by cash received from investment income, milestones, and research payments from our collaborative partners.

Investing activities generated \$36,351,000 in year 2002, compared with cash used of \$44,269,000 in year 2001. Our capital expenditures declined \$731,000 in 2002, compared with 2001. The cash generated by investing activities during 2002 reflects the use of invested funds to finance ongoing operations.

Cash generated by financing activities in year 2002 was \$486,000, compared with cash generated in year 2001 of \$19,043,000. Year 2001 included proceeds from the exercise of publicly traded warrants in January 2001, for net proceeds of \$20,143,000 and proceeds from the exercise of employee stock options and other warrants for proceeds of \$502,000, partially reduced by the acquisition of 213,000 shares of treasury stock for total proceeds of \$1,602,000. During 2002, we generated \$486,000 in cash from the proceeds of stock option exercises, and the sale of common stock at market price to our new CEO.

#### *Material Commitments*

Our only material contractual commitments are comprised of a loan commitment to Revotar and office and laboratory facility leases. We and the minority shareholders of Revotar have committed to lend Revotar approximately \$4.5 million of which our commitment will be approximately \$3.4 million. The terms of the loans require quarterly interest payments and repayment of all principal on or before April 1, 2007, subject to certain loan provisions regarding profitability or liquidity. Our portion of the loan is denominated in U.S. dollars at an interest rate of seven percent fixed for the first two years and resets to the greater of seven percent or U.S. prime plus two and one-half percent on April 1, 2004. It is likely that Revotar may need to seek additional funding through collaborative arrangements and/or through public or private financings.

The Company had long-term obligations under our office and laboratory leases as follows (in thousands):

Contractual Obligations	Total	Less than 1 year	1-3 years	4-5 years	After 5 years
Operating Leases	\$4,873	\$1,616	\$3,126	\$131	---

## Outlook for 2003

In 2003, we expect to have the following results:

Net Sales of Argatroban by GSK .....	\$30.0 to \$35.0 million
Revenues .....	\$10.5 to \$12.0 million
Expenses (net of Revotar minority interest) .....	\$42.0 to \$45.0 million
Investment Income .....	\$0.9 to \$1.1 million
Estimated Net Loss .....	\$30.0 to \$33.0 million
Cash and Investments at Year End .....	\$32.0 to \$35.0 million

In January 2003, ICOS announced that it had reached a conclusion that joint development of the endothelin receptor antagonist program by ICOS-TBC should not continue. ICOS and TBC are currently negotiating the terms pursuant to which TBC could independently continue the program. The financial terms of this transaction are subject to ongoing negotiations between the two companies. If we are successful in reaching an agreement, it is likely that we will be responsible for 100% of development expenses incurred after January 1, 2003 related to the endothelin receptor antagonist program, which we believe will be between \$19 million and \$21 million in 2003. A delay in reaching an agreement with ICOS could adversely affect or delay the development of the endothelin receptor antagonist program.

Our estimates of results for 2003 will be impacted by the financial terms of the ongoing negotiations between ICOS and us.

### Longer-Term Outlook

We expect to incur substantial research and development expenditures as we design and develop biopharmaceutical products for the prevention and treatment of cardiovascular and other diseases. We anticipate that our operating expenses will increase in subsequent years because:

- We expect to incur significant expenses in conjunction with additional clinical trial costs for sitaxsentan and research and clinical trial costs for development of bimosiamose compounds and expect to begin to incur costs for clinical trials related to additional compounds. These costs include:
  - hiring personnel to direct and carry out all operations related to clinical trials;
  - hospital and procedural costs;
  - services of a contract research organization; and
  - purchasing and formulating large quantities of the compound to be used in such trials.
- There may be additional costs in future periods related to Argatroban in complying with ongoing FDA requirements and possible clinical trial expenditures for additional therapeutic indications.
- Our administrative costs and costs to commercialize our products will increase as our products are further developed and marketed.

We have been unprofitable to date and expect to incur operating losses for the next several years as we invest in product research and development, preclinical and clinical testing and regulatory compliance. We will require substantial additional funding to complete the research and development of our product candidates, to establish commercial scale manufacturing facilities, if necessary, and to market our products. Estimates of our future capital requirements will depend on many factors, including:

- market acceptance and commercial success of Argatroban;
- expenses and risks associated with clinical trials to expand the indications for Argatroban;

- continued scientific progress in our drug discovery programs;
- the magnitude of these programs;
- progress with preclinical testing and clinical trials;
- the time and costs involved in obtaining regulatory approvals;
- the costs involved in filing, prosecuting and enforcing patent claims;
- competing technological and market developments and changes in our existing research relationships;
- our ability to maintain and establish additional collaborative arrangements; and
- effective commercialization activities and arrangements.

Subject to these factors, we anticipate that our existing capital resources and other revenue sources, should be sufficient to fund our cash requirements through year 2004. Notwithstanding revenues, which may be produced through sales of potential future products, if approved, we anticipate that we will need to secure additional funds to continue the required levels of research and development to reach our long-term goals. We intend to seek such additional funding through collaborative arrangements and/or through public or private financings.

In 2002, the stockholders of Revotar executed an agreement to provide approximately \$4.5 million in unsecured loans, of which our commitment was approximately \$3.4 million. Under the loan agreement, we have advanced approximately \$1.2 million to Revotar during 2002. We believe that Revotar's existing funds, the remaining commitments under the loan agreement and proceeds under German government scientific grants will be sufficient to fund Revotar into the first quarter of 2004. In order to continue to operate beyond that time, Revotar will need to seek additional funding through collaborative arrangements and/or through public or private financings in the future.

#### *Off-Balance Sheet Arrangements*

We do not engage in off-balance sheet financing arrangements; however we have been obligated to fund our proportionate share (50%) of any contractual obligations of ICOS-TBC. After December 31, 2002, we are responsible for funding 100% of the expenses of ICOS-TBC. After December 31, 2002, ICOS-TBC is not obligated for any leases, long-term debt, or other fixed obligations.

#### **Impact of Inflation and Changing Prices**

The pharmaceutical research industry is labor intensive, and wages and related expenses increase in inflationary periods. The lease of space and related building services for the Houston facility contains a clause that escalates rent and related services each year based on the increase in building operating costs and the increase in the Houston Consumer Price Index, respectively. To date, inflation has not had a significant impact on our operations.

### **ITEM 7A — QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK**

#### **Foreign Currency Exchange Risk**

We are exposed to market risk primarily from changes in foreign currency exchange rates. The following describes the nature of this risk that is not believed to be material to us.

We have a majority-owned affiliate in Berlin, Germany and consolidate the results of operations into our consolidated financial results. Although not material to date, our reported expenses and cash flows from this affiliate are exposed to changing exchange rates. We also have contracts with entities in other areas outside the U.S. that are denominated in a foreign currency. To date, these currencies have not fluctuated materially. During 2003, Revotar engaged in a program of hedging the effect of foreign currency fluctuations on approximately \$1.6 million in future loan payments from us.

**ITEM 8 — FINANCIAL STATEMENTS AND SUPPLEMENTAL DATA**

The financial statements we are required to include in this Item 8 are set forth in Item 15 of this Form 10-K.

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

Not applicable.

### PART III

#### **ITEM 10 — DIRECTORS AND EXECUTIVE OFFICERS**

Incorporated herein by reference to the Company's definitive Proxy Statement for the Annual Meeting of Stockholders to be held on May 16, 2003.

#### **ITEM 11 — EXECUTIVE COMPENSATION**

Incorporated herein by reference to the Company's definitive Proxy Statement for the Annual Meeting of Stockholders to be held on May 16, 2003.

#### **ITEM 12 — SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT**

Incorporated herein by reference to the Company's definitive Proxy Statement for the Annual Meeting of Stockholders to be held on May 16, 2003.

#### **ITEM 13 — CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS**

Incorporated herein by reference to the Company's definitive Proxy Statement for the Annual Meeting of Stockholders to be held on May 16, 2003.

#### **ITEM 14 — CONTROLS AND PROCEDURES**

##### **(a) Evaluation of disclosure controls and procedures**

Our chief executive officer and our vice president, finance and administration, after evaluating the effectiveness of our "disclosure controls and procedures" (as defined in Exchange Act Rules 13a-14(c) and 15d-14(c)) as of a date (the "Evaluation Date") within 90 days prior to the filing date of this annual report on Form 10-K, have concluded that, as of the Evaluation Date, our disclosure controls and procedures were adequate to ensure that material information relating to the registrant and its consolidated subsidiaries would be made known to them by others within those entities.

##### **(b) Changes in internal controls**

To our knowledge, there were no significant changes in our internal controls or in other factors that could significantly affect internal controls subsequent to the Evaluation Date.

## PART IV

### ITEM 15 — EXHIBITS, FINANCIAL STATEMENTS, SCHEDULES AND REPORTS ON FORM 8-K

#### (a) 1. Index to Consolidated Financial Statements

Reference is made to the Consolidated Financial Statements, the reports thereon, and the notes thereto commencing at Page F-1 of this Annual Report on Form 10-K. Set forth below is an index to such Financial Statements.

	<u>Page</u>
Independent Auditors' Report .....	F-1
Consolidated Balance Sheets .....	F-2
Consolidated Statements of Operations and Comprehensive Loss .....	F-3
Consolidated Statements of Stockholders' Equity .....	F-4
Consolidated Statements of Cash Flows .....	F-6
Notes to Consolidated Financial Statements .....	F-7

#### 2. Financial Statement Schedules

##### Independent Auditors' Report

Balance Sheets of ICOS-Texas Biotechnology L.P. (A Development Stage Limited partnership) as of December 31, 2002 and 2001, and the related statements of operations, statements of partners' deficit and cash flows for each of the years in the two-year period ended December 31, 2002, the period from June 6, 2000 (inception) through December 31, 2000 and the period from June 6, 2000 (inception) through December 31, 2002, and notes thereto.

All other schedules have been omitted since the information is not required or is not material to require submission of the schedule, or because the information is included in the financial statements or the notes thereto.

#### 3. Index to Exhibits

Information with respect to this Item is contained in the attached Index to Exhibits.

The Company will furnish a copy of any one or more of these exhibits to a shareholder who so requests upon receipt of payment for the costs of duplication and mailing the requested item.

#### (b) Reports on Form 8-K

Four reports on Form 8-K were filed during the quarter ended December 31, 2002. A report on Form 8-K dated October 2, 2002 was filed regarding the preliminary results for the use of Argatroban as a treatment for acute ischemic stroke. A report on Form 8-K dated October 21, 2002 was filed regarding the phase 2b/3 trial results for Sitaxsentan. A report on Form 8-K dated November 7, 2002 was filed regarding the Company's third quarter 2002 financial results, market growth for Argatroban and clinical trial status. A report on Form 8-K dated December 19, 2002 was filed regarding an update to shareholders on Sitaxsentan trials and sales of Argatroban.

All schedules have been omitted since the information is not required or is not material to require submission of the schedule, or because the information is included in the financial statements or the notes thereto.

(d) Financial Statements of 50-Percent-or-Less Owned Persons

**ICOS – TEXAS BIOTECHNOLOGY L.P.**  
**(A DEVELOPMENT STAGE LIMITED PARTNERSHIP)**

**Table of Contents**

Independent Auditors' Report

Balance Sheets as of December 31, 2002 and 2001

Statements of Operations for each of the years in the two-year period ended December 31, 2002, the period from June 6, 2000 (inception) through December 31, 2000, and the period from June 6, 2000 (inception) through December 31, 2002

Statements of Partners' Deficit for each of the years in the two-year period ended December 31, 2002, and the period from June 6, 2000 (inception) through December 31, 2000

Statements of Cash Flows for each of the years in the two-year period ended December 31, 2002, the period from June 6, 2000 (inception) through December 31, 2000, and the period from June 6, 2000 (inception) through December 31, 2002

Notes to Financial Statements



## Independent Auditors' Report

The Board of Directors  
ICOS – Texas Biotechnology L.P.:

We have audited the accompanying balance sheets of ICOS – Texas Biotechnology L.P. (a development stage limited partnership) as of December 31, 2002 and 2001, and the related statements of operations, partners' deficit and cash flows for each of the years in the two-year period ended December 31, 2002, the period from June 6, 2000 (inception) to December 31, 2000, and the period from June 6, 2000 (inception) to December 31, 2002. These financial statements are the responsibility of the Partnership's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with auditing standards generally accepted in the United States of America. 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 includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of ICOS – Texas Biotechnology L.P. as of December 31, 2002 and 2001, and the results of its operations and its cash flows for each of the years in the two-year period ended December 31, 2002, the period from June 6, 2000 (inception) to December 31, 2000, and the period from June 6, 2000 (inception) to December 31, 2002, in conformity with accounting principles generally accepted in the United States of America.

The accompanying financial statements have been prepared assuming that ICOS – Texas Biotechnology L.P. will continue as a going concern. As discussed in note 6 to the financial statements, ICOS – Texas Biotechnology L.P. has experienced recurring losses from operations and has a partners' deficit which raise substantial doubt about its ability to continue as a going concern. Management's plans in regard to these matters are also described in note 6. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

/s/ KPMG LLP

Seattle, Washington  
January 30, 2003

**ICOS - TEXAS BIOTECHNOLOGY L.P.**  
**(A DEVELOPMENT STAGE LIMITED PARTNERSHIP)**

**BALANCE SHEETS**

	(in thousands)	
	December 31,	
	<u>2002</u>	<u>2001</u>
<b>ASSETS</b>		
Current assets – cash.....	\$ 1	\$ 1
<b>LIABILITIES AND PARTNERS' DEFICIT</b>		
Current liabilities - accrued expenses payable to partners	\$ 5,235	\$ 7,059
Partners' deficit:		
General partner interests:		
ICOS-ET-GP LLC.....	(47)	(30)
TBC-ET, Inc. ....	(47)	(30)
Limited partner interests:		
ICOS-ET-LP LLC.....	(2,570)	(3,499)
Texas Biotechnology Corporation.....	(2,570)	(3,499)
Total partner's deficit .....	<u>(5,234)</u>	<u>(7,058)</u>
	<u>\$ 1</u>	<u>\$ 1</u>

**ICOS - TEXAS BIOTECHNOLOGY L.P.**  
(A DEVELOPMENT STAGE LIMITED PARTNERSHIP)

STATEMENTS OF OPERATIONS

	(in thousands)			
	Year ended December 31, 2002	Year ended December 31, 2001	Period from June 6, 2000 (inception) through December 31, 2000	Period from June 6, 2000 (inception) through December 31, 2002
Revenue	\$ -	\$ -	\$ 547	\$ 547
Operating expenses:				
Research and development:				
Contributed technology license from				
Texas Biotechnology Corporation	-	4,000	4,000	8,000
Texas Biotechnology Corporation	2,312	6,190	4,706	13,208
ICOS Corporation	14,321	12,682	2,809	29,812
General and administrative:				
Texas Biotechnology Corporation	153	-	-	153
ICOS Corporation	330	26	8	364
Total operating expenses	17,116	22,898	11,523	51,537
Net loss	\$ (17,116)	\$ (22,898)	\$ (10,976)	\$ (50,990)

**ICOS - TEXAS BIOTECHNOLOGY L.P.**  
(A DEVELOPMENT STAGE LIMITED PARTNERSHIP)

STATEMENTS OF PARTNERS' DEFICIT

	(in thousands)				
	ICOS-ET-GP LLC	TBC-ET, Inc.	ICOS-ET-LP LLC	Texas Biotechnology Corporation	Partners' Deficit
<b>Balances at June 6, 2000 (inception)</b>	\$ -	\$ -	\$ -	\$ -	\$ -
Partner contributions:					
Cash	4	4	4,031	2,031	6,070
Technology license	-	-	-	4,000	4,000
Capital distribution	-	-	-	(2,000)	(2,000)
Net loss	(11)	(11)	(5,477)	(5,477)	(10,976)
<b>Balances at December 31, 2000</b>	(7)	(7)	(1,446)	(1,446)	(2,906)
Partner contributions:					
Cash	-	-	9,373	7,373	16,746
Technology license	-	-	-	4,000	4,000
Capital distribution	-	-	-	(2,000)	(2,000)
Net loss	(23)	(23)	(11,426)	(11,426)	(22,898)
<b>Balances at December 31, 2001</b>	(30)	(30)	(3,499)	(3,499)	(7,058)
Partner contributions:					
Cash	-	-	9,470	9,470	18,940
Net loss	(17)	(17)	(8,541)	(8,541)	(17,116)
<b>Balances at December 31, 2002</b>	\$ (47)	\$ (47)	\$ (2,570)	\$ (2,570)	\$ (5,234)

**ICOS - TEXAS BIOTECHNOLOGY L.P.**  
**(A DEVELOPMENT STAGE LIMITED PARTNERSHIP)**

**STATEMENTS OF CASH FLOWS**

	(in thousands)			
	Year ended December 31, 2002	Year ended December 31, 2001	Period from June 6, 2000 (inception) through December 31, 2000	Period from June 6, 2000 (inception) through December 31, 2002
<b>Cash flows from operating activities:</b>				
Net loss	\$ (17,116)	\$ (22,898)	\$ (10,976)	\$ (50,990)
Adjustments to reconcile net loss to net cash used in operating activities:				
Contributed technology license	-	4,000	4,000	8,000
Change in operating assets and liabilities:				
Receivable from Texas Biotechnology Corporation	-	470	(470)	-
Accrued expenses payable to partners	(1,824)	3,662	3,397	5,235
Net cash used in operating activities	<u>(18,940)</u>	<u>(14,766)</u>	<u>(4,049)</u>	<u>(37,755)</u>
<b>Cash flows from financing activities:</b>				
Partner contributions	18,940	16,746	6,070	41,756
Capital distributions	-	(2,000)	(2,000)	(4,000)
Net cash provided by financing activities	<u>18,940</u>	<u>14,746</u>	<u>4,070</u>	<u>37,756</u>
Net increase (decrease) in cash	-	(20)	21	1
Cash at beginning of period	<u>1</u>	<u>21</u>	<u>-</u>	<u>-</u>
Cash at end of period	<u>\$ 1</u>	<u>\$ 1</u>	<u>\$ 21</u>	<u>\$ 1</u>

**ICOS – TEXAS BIOTECHNOLOGY L.P.**  
**(A DEVELOPMENT STAGE LIMITED PARTNERSHIP)**

Notes to Financial Statements

December 31, 2002 and 2001

*(Dollars in thousands, unless otherwise noted)*

**(1) Organization and Business Operations**

ICOS-Texas Biotechnology L.P. (the "Partnership"), is a development stage limited partnership that was formed on June 6, 2000 by Texas Biotechnology Corporation, a Delaware corporation ("TBC"), and ICOS-ET-LP LLC, a Washington limited liability company ("ICOS-LP"), as limited partners, and TBC-ET, Inc., a Delaware corporation ("TBC-GP"), and ICOS-ET-GP LLC, a Washington limited liability company ("ICOS-GP"), as general partners. The Partnership was organized to develop and globally commercialize endothelin receptor antagonists. The Partnership is managed jointly by TBC-GP and ICOS-GP. Profits, losses and distributions, except for distributions for payment of TBC's exclusive license (see Note 3), are allocated based on respective ownership interests. ICOS Corporation ("ICOS") is the sole member of both ICOS-LP and ICOS-GP. TBC is the sole member of TBC-GP. Both TBC and ICOS provide the Partnership with research and development services.

**(2) Summary of Significant Accounting Policies**

**(a) Use of Estimates in the Preparation of Financial Statements**

The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, 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. Actual results could differ from those estimates.

**(b) Revenue Recognition**

Revenue represents research payments received by TBC, which were assigned to the Partnership and recognized as the related services were performed.

**(c) Research and Development Costs**

Research and development costs are expensed as incurred.

**(d) Income Taxes**

No Federal income tax expense or benefit is included in the financial statements since such taxes, if any, are payable or recoverable by each partner.

**(e) Operating Segments**

The Partnership has one operating segment, the development and commercialization of endothelin receptor antagonist products for human therapeutic use.

**ICOS - TEXAS BIOTECHNOLOGY L.P.**  
**(A DEVELOPMENT STAGE LIMITED PARTNERSHIP)**  
Notes to Financial Statements

December 31, 2002 and 2001  
*(Dollars in thousands, unless otherwise noted)*

**(3) Equity Transactions**

TBC made an initial capital contribution to the Partnership of an exclusive worldwide license of intellectual property associated with endothelin receptor antagonists, including patent rights and technical information, and ICOS-LP made an initial capital contribution to the Partnership of \$2 million in cash. In exchange for their contributions, each party received a 49.9% limited partnership interest in the Partnership. ICOS-GP and TBC-GP each contributed \$4 in exchange for a .1% general partnership interest in the Partnership.

The technology license contributed to the Partnership by TBC was initially valued at \$4 million, based on the cash contribution from ICOS-LP and the concurrent capital distribution to TBC discussed below. The contributed valuation of the technology license increased by \$4 million in 2001, upon the achievement of certain development objectives, and may increase by up to \$103 million in the future, if certain additional milestones are achieved as provided for in the Agreement of Limited Partnership of ICOS-Texas Biotechnology L.P. (the "Agreement").

Under the terms of the Agreement, TBC received a capital distribution of \$2 million in conjunction with formation of the Partnership and received an additional \$2 million capital distribution in October 2001 upon the achievement of certain development objectives.

**(4) License Agreements**

In connection with TBC's initial capital contribution, the Partnership entered into an Endothelin License Agreement with TBC, subject to the rights of an agreement with LG Chemical, Ltd. discussed below. Under the Endothelin License Agreement, the Partnership received an exclusive right and license to certain proprietary patent rights, technical information, technology and know-how relating to, and useful in, the manufacture, production and worldwide commercial sale of endothelin products for human therapeutic use. The value of the license was charged to development expense as the underlying technology represented incomplete product research and development.

In October 1996, TBC entered into a Strategic Alliance Agreement with LG Chemical, Ltd. ("LG Chem"), a Korean corporation, (the "LG Chem Agreement"), pursuant to which TBC granted LG Chem certain technology rights and agreed to perform certain research and development activities on behalf of LG Chem in exchange for the right to receive research and royalty payments in the future.

In conjunction with its formation, the Partnership was assigned and assumed certain of TBC's rights and obligations under the LG Chem Agreement. During 2000, the Partnership recognized \$547 in revenue associated with services performed under the LG Chem Agreement. The LG Chem Agreement was terminated during 2001. The Partnership will not recognize any further revenue or receive any additional payments, and has no further obligations, under the LG Chem Agreement.

**(5) Research and Development Service Agreement**

In June 2000, the Partnership entered into a Research and Development Service Agreement (the "R&D Agreement") with TBC and ICOS, pursuant to which TBC and ICOS agreed to provide research and development services for, and on behalf of, the Partnership. The Partnership reimburses TBC and ICOS, at a per-hour amount, calculated on the basis of actual hours incurred by TBC and ICOS, plus certain development and administrative expenses. There is no minimum commitment for research and development, and the Partnership can contract with other parties to provide research and development services.

**(6) Financing**

ICOS-TBC has experienced recurring losses from operations and has a partners' deficit of \$5.2 million at December 31, 2002, which raise substantial doubt about its ability to continue as a going concern.

Pursuant to the Agreement, except as modified by a subsequent Letter Agreement between ICOS and TBC dated February 14, 2003 (the "Letter Agreement"), ongoing activities of the Partnership are to be funded by the limited partners in relation

**ICOS - TEXAS BIOTECHNOLOGY L.P.**  
**(A DEVELOPMENT STAGE LIMITED PARTNERSHIP)**  
Notes to Financial Statements

December 31, 2002 and 2001

*(Dollars in thousands, unless otherwise noted)*

to their limited partnership interests. Substantially all of the partners' deficit at December 31, 2002, was funded by capital contributions from the limited partners during the first quarter of 2003.

Pursuant to the Letter Agreement, TBC has agreed to be responsible for 100% of all costs and expenses of the Partnership incurred after December 31, 2002, through June 30, 2003, or earlier termination of the Letter Agreement upon mutual consent of both parties.

In January 2003, ICOS announced its conclusion that joint development of the endothelin receptor antagonist program, through the Partnership, should not continue. ICOS and TBC continue to negotiate the terms pursuant to which TBC might independently continue the endothelin receptor antagonist program.



## SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Houston and State of Texas on the 27<sup>th</sup> day of March, 2003.

### TEXAS BIOTECHNOLOGY CORPORATION

By: /s/ STEPHEN L. MUELLER  
Stephen L. Mueller  
*Vice President, Finance and Administration,  
Secretary and Treasurer*

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons and in the capacities indicated on the 27<sup>th</sup> day of March, 2003.

<u>Signature</u>	<u>Title</u>
<u>/s/ JOHN M. PIETRUSKI</u> John M. Pietruski	Chairman of the Board of Directors
<u>/s/ BRUCE D. GIVEN</u> Bruce D. Given, M.D.	Director, President and Chief Executive Officer (Principal Executive Officer)
<u>/s/ RICHARD A.F. DIXON</u> Richard A.F. Dixon, Ph.D.	Director and Senior Vice President, Research and Chief Scientific Officer
<u>/s/ STEPHEN L. MUELLER</u> Stephen L. Mueller	Vice President, Finance and Administration, Secretary and Treasurer (Principal Financial and Accounting Officer)
<u>/s/ RON J. ANDERSON</u> Ron J. Anderson, M.D.	Director
<u>/s/ FRANK C. CARLUCCI</u> Frank C. Carlucci	Director
<u>/s/ ROBERT J. CRUIKSHANK</u> Robert J. Cruikshank	Director
<u>/s/ SUZANNE OPARIL</u> Suzanne Oparil, M.D.	Director
<u>/s/ WILLIAM R. RINGO, JR.</u> William R. Ringo, Jr.	Director
<u>/s/ JAMES A. THOMSON</u> James A. Thomson, Ph.D.	Director
<u>/s/ JAMES T. WILLERSON</u> James T. Willerson, M.D.	Director

## Certifications

I, Bruce D. Given, M.D., certify that:

1. I have reviewed this annual report on Form 10-K of Texas Biotechnology Corporation;
2. Based on my knowledge, this annual report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this annual report;
3. Based on my knowledge, the financial statements, and other financial information included in this annual report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this annual report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-14 and 15d-14) for the registrant and we have:
  - a) designed such disclosure controls and procedures to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this annual report is being prepared;
  - b) evaluated the effectiveness of the registrant's disclosure controls and procedures as of a date within 90 days prior to the filing date of this annual report ("Evaluation Date"); and
  - c) presented in this annual report our conclusions about the effectiveness of the disclosure controls and procedures based on our evaluation as of the Evaluation Date;
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation, to the registrant's auditors and the audit committee of the registrant's board of directors [or persons performing the equivalent function]:
  - a) all significant deficiencies in the design or operation of internal controls which could adversely affect the registrant's ability to record, process, summarize and report financial data and have identified for the registrant's auditors any material weaknesses in internal controls; and
  - b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal controls; and
6. The registrant's other certifying officer and I have indicated in this annual report whether or not there were significant changes in internal controls or in other factors that could significantly affect internal controls subsequent to our most recent evaluation, including any corrective actions with regard to significant deficiencies and material weaknesses.

Date: March 27, 2003

By /s/ Bruce D. Given, M.D.  
Bruce D. Given, M.D.  
President and Chief Executive Officer

## Certifications

I, Stephen L. Mueller, certify that:

1. I have reviewed this annual report on Form 10-K of Texas Biotechnology Corporation;
2. Based on my knowledge, this annual report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this annual report;
3. Based on my knowledge, the financial statements, and other financial information included in this annual report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this annual report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-14 and 15d-14) for the registrant and we have:
  - a) designed such disclosure controls and procedures to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this annual report is being prepared;
  - b) evaluated the effectiveness of the registrant's disclosure controls and procedures as of a date within 90 days prior to the filing date of this annual report ("Evaluation Date"); and
  - c) presented in this annual report our conclusions about the effectiveness of the disclosure controls and procedures based on our evaluation as of the Evaluation Date;
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation, to the registrant's auditors and the audit committee of the registrant's board of directors [or persons performing the equivalent function]:
  - a) all significant deficiencies in the design or operation of internal controls which could adversely affect the registrant's ability to record, process, summarize and report financial data and have identified for the registrant's auditors any material weaknesses in internal controls; and
  - b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal controls; and
6. The registrant's other certifying officer and I have indicated in this annual report whether or not there were significant changes in internal controls or in other factors that could significantly affect internal controls subsequent to our most recent evaluation, including any corrective actions with regard to significant deficiencies and material weaknesses.

Date: March 27, 2003

By /s/ Stephen L. Mueller  
Stephen L. Mueller  
Vice President, Finance and Administration  
Secretary and Treasurer

[THIS PAGE INTENTIONALLY LEFT BLANK]

## INDEPENDENT AUDITORS' REPORT

The Board of Directors  
Texas Biotechnology Corporation:

We have audited the accompanying consolidated balance sheets of Texas Biotechnology Corporation and subsidiaries (the "Company") as of December 31, 2002 and 2001, and the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows for each of the years in the three-year period ended December 31, 2002. These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated financial statements based on our audits.

We conducted our audits in accordance with auditing standards generally accepted in the United States of America. 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 includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of Texas Biotechnology Corporation and subsidiaries as of December 31, 2002 and 2001, and the results of their operations and their cash flows for each of the years in the three-year period ended December 31, 2002, in conformity with accounting principles generally accepted in the United States of America.

/s/ KPMG LLP

Houston, Texas  
March 5, 2003

**TEXAS BIOTECHNOLOGY CORPORATION AND SUBSIDIARIES**

**CONSOLIDATED BALANCE SHEETS**

(\$ in thousands, except share data)

<u>ASSETS</u>	<u>December 31,</u>	
	<u>2002</u>	<u>2001</u>
Current assets:		
Cash and cash equivalents .....	\$ 21,228	\$ 10,086
Short-term investments .....	26,533	46,465
Accounts receivable .....	1,098	655
Other current receivables .....	473	618
Receivable from related party under collaborative arrangement .....	393	1,144
Prepays .....	1,482	1,350
Total current assets .....	51,207	60,318
Long-term investments .....	20,244	38,876
Equipment and leasehold improvements, net .....	5,579	4,300
Other assets .....	762	868
Total assets .....	\$ 77,792	\$ 104,362
<u>LIABILITIES AND STOCKHOLDERS' EQUITY</u>		
Current liabilities:		
Accounts payable .....	\$ 950	\$ 2,187
Accrued expenses .....	3,774	3,902
Deferred revenue from related party .....	591	1,159
Deferred revenue from unrelated parties .....	927	748
Total current liabilities .....	6,242	7,996
Liability to related party .....	2,664	3,533
Deferred revenue from related party .....	1,181	1,722
Deferred revenue from unrelated parties .....	3,019	3,041
Minority interest in Revotar .....	2,608	3,833
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, par value \$.005 per share. At December 31, 2002 and December 31, 2001, 5,000,000 shares authorized; none outstanding. ....	---	---
Common stock, par value \$.005 per share. At December 31, 2002, 75,000,000 shares authorized; 44,015,364 shares issued. At December 31, 2001, 75,000,000 shares authorized, 43,783,638 shares issued.....	220	218
Additional paid-in capital .....	211,847	210,616
Deferred compensation expense .....	(223)	---
Treasury stock, 213,000 shares at December 31, 2002 and 2001 .....	(1,602)	(1,602)
Accumulated other comprehensive income (loss) .....	1	(299)
Accumulated deficit .....	(148,165)	(124,696)
Total stockholders' equity .....	62,078	84,237
Total liabilities and stockholders' equity .....	\$ 77,792	\$ 104,362

See accompanying notes to consolidated financial statements.

**TEXAS BIOTECHNOLOGY CORPORATION AND SUBSIDIARIES**

**CONSOLIDATED STATEMENTS OF OPERATIONS  
AND COMPREHENSIVE LOSS**

(\$ in thousands, except per share data)

	Year Ended December 31,		
	2002	2001	2000
Revenues:			
Research agreements .....	\$ 3,570	\$ 4,342	\$ 3,889
Collaborative research and development from ICOS-TBC, L.P. ....	1,090	1,442	1,123
Royalty income .....	3,514	1,586	234
License fees, milestones and grants .....	2,259	1,547	10,446
Total revenues .....	10,433	8,917	15,692
Expenses:			
Research and development .....	20,066	17,861	13,513
Equity in loss of ICOS-TBC, L.P. ....	8,557	9,450	3,487
General and administrative .....	8,976	6,733	6,552
Total expenses .....	37,599	34,044	23,552
Operating loss .....	(27,166)	(25,127)	(7,860)
Investment income, net .....	2,472	5,236	4,362
Loss before minority interest and cumulative effect of change in accounting principle .....	(24,694)	(19,891)	(3,498)
Minority interest in loss of Revotar .....	1,225	749	209
Loss before cumulative effect of change in accounting principle .....	(23,469)	(19,142)	(3,289)
Cumulative effect of change in accounting principle .....	---	---	(2,366)
Net loss applicable to common shares .....	\$ (23,469)	\$ (19,142)	\$ (5,655)
Other comprehensive income:			
Unrealized income (loss) on foreign currency translation .....	300	(284)	(15)
Comprehensive loss .....	\$ (23,169)	\$ (19,426)	\$ (5,670)
Net loss per share basic and diluted .....	\$ (0.54)	\$ (0.44)	\$ (0.14)
Weighted average common shares used to compute net loss per share basic and diluted .....	43,741	43,637	39,150

See accompanying notes to consolidated financial statements.

TEXAS BIOTECHNOLOGY CORPORATION AND SUBSIDIARIES

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY

For the years ended December 31, 2002, 2001 and 2000

(\$ in thousands)

	Common stock		Additional paid-in capital	Treasury stock	Accumulated other comprehensive income (loss)	Accumulated deficit	Total Stockholders' equity
	Shares	Amount					
Balance at January 1, 2000 .....	34,392,909	\$ 172	\$ 118,317	\$ ---	\$ ---	\$ (99,899)	\$ 18,590
Issuance of common stock in public offering.....	5,584,591	28	65,206	---	---	---	65,234
Issuance of common stock for stock option exercises .....	618,904	3	2,319	---	---	---	2,322
Issuance of common stock for warrant exercises.....	531,128	3	2,537	---	---	---	2,540
Issuance of common stock in payment of expenses.....	2,236	---	30	---	---	---	30
Issuance of common stock in payment for consulting services .....	2,000	---	16	---	---	---	16
Issuance of common stock in payment for research and development.....	71,429	---	965	---	---	---	965
Net loss .....	---	---	---	---	---	(5,655)	(5,655)
Other comprehensive loss .....	---	---	---	---	(15)	---	(15)
Balance at December 31, 2000.....	<u>41,203,197</u>	<u>\$ 206</u>	<u>\$ 189,390</u>	<u>\$ ---</u>	<u>\$ (15)</u>	<u>\$ (105,554)</u>	<u>\$ 84,027</u>
Issuance of common stock for stock option exercises .....	12,268	---	52	---	---	---	52
Issuance of common stock for warrant exercises.....	2,511,558	12	20,581	---	---	---	20,593
Issuance of common stock in payment of expenses.....	56,615	---	530	---	---	---	530
Compensation expense related to stock options .....	---	---	63	---	---	---	63
Purchase of treasury shares (213,000 shares).....	---	---	---	(1,602)	---	---	(1,602)
Net loss .....	---	---	---	---	---	(19,142)	(19,142)
Other comprehensive loss .....	---	---	---	---	(284)	---	(284)
Balance at December 31, 2001.....	<u>43,783,638</u>	<u>\$ 218</u>	<u>\$ 210,616</u>	<u>\$ (1,602)</u>	<u>\$ (299)</u>	<u>\$ (124,696)</u>	<u>\$ 84,237</u>

(Continued)



TEXAS BIOTECHNOLOGY CORPORATION AND SUBSIDIARIES

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY

For the years ended December 31, 2002, 2001 and 2000

(\$ in thousands)

	Common stock		Additional paid-in capital	Deferred compensation expense	Treasury stock	Accumulated other comprehensive income (loss)	Accumulated deficit	Total Stockholders' equity
	Shares	Amount						
Balance at December 31, 2001.....	43,783,638	\$ 218	\$ 210,616	\$ ---	\$ (1,602)	\$ (299)	\$ (124,696)	\$ 84,237
Issuance of common stock for								
stock option exercises .....	129,860	1	454		---	---	---	455
Issuance of common stock for								
warrant exercises.....	500	---	---		---	---	---	---
Sale of unregistered								
common stock .....	5,000	---	31		---	---	---	31
Issuance of common stock in								
payment of expenses .....	51,429	1	271		---	---	---	272
Compensation expense related to								
stock options .....	---	---	202	---	---	---	---	202
Amortization of deferred								
compensation expense.....	---	---	---	85	---	---	---	85
Deferred compensation expense								
related to issuance of stock....	50,000	---	308	(308)	---	---	---	---
Cancellation of restricted shares ....	(5,063)	---	(35)	---	---	---	---	(35)
Net loss .....	---	---	---	---	---	---	(23,469)	(23,469)
Other comprehensive income.....	---	---	---	---	---	300	---	300
Balance at December 31, 2002.....	<u>44,015,364</u>	<u>\$ 220</u>	<u>\$ 211,847</u>	<u>\$ (223)</u>	<u>\$ (1,602)</u>	<u>\$ 1</u>	<u>\$ (148,165)</u>	<u>\$ 62,078</u>

See accompanying notes to consolidated financial statements.

**TEXAS BIOTECHNOLOGY CORPORATION AND SUBSIDIARIES**

**CONSOLIDATED STATEMENTS OF CASH FLOWS**

(\$ in thousands)

	<u>Year Ended December 31,</u>		
	<u>2002</u>	<u>2001</u>	<u>2000</u>
<b>Cash flows from operating activities:</b>			
Net loss .....	\$ (23,469)	\$ (19,142)	\$ (5,655)
Adjustments to reconcile net loss to net cash (used in) provided by operating activities:			
Depreciation and amortization .....	1,071	913	998
Equity in loss of ICOS-TBC, L.P. ....	8,557	9,450	3,487
Minority interest in loss of Revotar .....	(1,225)	(749)	(209)
Expenses paid with stock .....	272	530	46
Compensation expense related to stock options .....	252	63	---
Loss on disposition of fixed assets .....	---	12	9
Decrease (increase) in interest receivable included in short-term and long-term investments .....	265	131	(558)
Changes in operating assets and liabilities:			
Increase in accounts receivable .....	(443)	(417)	(237)
(Increase) decrease in prepaids .....	(128)	(4)	104
Decrease in other current receivables .....	144	6	443
Decrease (increase) in receivable from related party under collaborative arrangement .....	751	(262)	(882)
(Decrease) increase in accounts payable and accrued expenses .....	(1,460)	1,533	2,342
Decrease in liability to related party .....	(9,426)	(7,293)	(2,110)
Increase in deferred revenue from unrelated parties .....	157	1,062	2,727
(Decrease) increase in deferred revenue from related party ..	(1,109)	1,187	1,693
Net cash (used in) provided by operating activities .....	<u>(25,791)</u>	<u>(12,980)</u>	<u>2,198</u>
<b>Cash flows from investing activities:</b>			
Purchases of equipment and leasehold improvements .....	(2,026)	(2,757)	(324)
Purchase of investments .....	(85,608)	(154,272)	(104,002)
Maturity of investments .....	123,985	112,760	72,996
Net cash provided by (used in) investing activities .....	<u>36,351</u>	<u>(44,269)</u>	<u>(31,330)</u>
<b>Cash flows from financing activities:</b>			
Acquisition of treasury stock .....	---	(1,602)	---
Contribution from minority interest in consolidated subsidiary ...	---	---	4,502
Proceeds from issuance of common stock and option and warrant exercises, net .....	486	20,645	70,096
Net cash provided by financing activities .....	<u>486</u>	<u>19,043</u>	<u>74,598</u>
Effect of exchange rate changes on cash .....	96	(178)	200
Net increase (decrease) in cash and cash equivalents .....	11,142	(38,384)	45,666
Cash and cash equivalents at beginning of year .....	10,086	48,470	2,804
Cash and cash equivalents at end of year .....	<u>\$ 21,228</u>	<u>\$ 10,086</u>	<u>\$ 48,470</u>
<b>Supplemental schedule of noncash financing activities:</b>			
Issuance of common stock for research and development, license fee and services .....	<u>\$ 272</u>	<u>\$ 530</u>	<u>\$ 1,011</u>

See accompanying notes to consolidated financial statements.

# TEXAS BIOTECHNOLOGY CORPORATION AND SUBSIDIARIES

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

### (1) Organization and Significant Accounting Policies

#### (a) Organization

Texas Biotechnology Corporation (the "Company" or "TBC"), a Delaware Corporation, is a biopharmaceutical company focused on the discovery, development and commercialization of novel synthetic small molecule compounds for the treatment of a variety of cardiovascular, vascular and related inflammatory diseases. Since its formation in 1989, the Company has been engaged principally in research and drug discovery programs and clinical development of certain drug compounds. On July 25, 1994, the Company acquired all of the outstanding common stock of ImmunoPharmaceutics, Inc. ("IPI") in exchange for common stock, par value \$.005 per share (the "Common Stock"), of the Company. On June 6, 2000, TBC, through its wholly owned subsidiary, TBC-ET, Inc., a Delaware Corporation, and ICOS Corporation, a Delaware Corporation, ("ICOS") entered into an agreement and formed ICOS-Texas Biotechnology L.P., a Delaware limited partnership ("ICOS-TBC"), to develop and globally commercialize endothelin-A receptor antagonists. TBC and ICOS are both 50% owners in ICOS-TBC. For further discussion of the ICOS-TBC partnership, see Note 8. During the third quarter of 2000, TBC formed Revotar Biopharmaceuticals AG ("Revotar"), a German corporation, to conduct research and development for novel small molecule compounds and to develop and commercialize TBC's selectin antagonists. The Company retained a majority interest in Revotar.

The Company is presently working on a number of long-term development projects that involve experimental and unproven technology, which may require many years and substantial expenditures to complete, and which may or may not be successful. Sales of the Company's first product, for which it receives royalty income, Argatroban, began during November 2000.

#### (b) Basis of Consolidation

The Company's consolidated financial statements include the accounts of the Company, its wholly owned subsidiaries, IPI and TBC-ET, Inc., and its majority controlled subsidiary, Revotar. All material intercompany balances and transactions have been eliminated.

# TEXAS BIOTECHNOLOGY CORPORATION AND SUBSIDIARIES

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

*(c) Cash, Cash Equivalents, Short-Term Investments and Long-Term Investments*

Cash equivalents are considered to be those securities or instruments with original maturities, when purchased, of three months or less. Short-term investments are those investments which have an original maturity of less than one year and greater than three months at the purchase date. Long-term investments consist of securities with a remaining maturity of one year or more. Cash equivalents, short-term and long-term investments are stated at cost plus accrued interest, which approximates market value. Interest income is accrued as earned. The Company classifies all short-term and long-term investments as held to maturity. Composition of cash and investments was as follows (in thousands):

	<u>December 31, 2002</u>	<u>December 31, 2001</u>
Cash and cash equivalents:		
Demand and money market accounts	\$ 609	\$ 690
Corporate commercial paper	20,619	9,396
Total cash and cash equivalents	\$ 21,228	\$ 10,086
Short-term investments:		
U.S. Government agency securities	\$ 3,999	\$ 817
Corporate commercial paper and loan participations	22,333	44,083
Time deposits	---	1,255
Accrued interest on above	201	310
Total short-term investments	\$ 26,533	\$ 46,465
Long-term investments:		
U.S. Government agency securities	\$ 12,000	\$ 30,989
Corporate commercial paper and loan participations	7,990	7,476
Accrued interest on above	254	411
Total long-term investments	\$ 20,244	\$ 38,876

*(d) Equipment and Leasehold Improvements*

Equipment and leasehold improvements are stated at cost less accumulated depreciation and amortization. Depreciation of furniture and equipment is provided on the straight-line method over the estimated useful lives of the respective assets (3 to 10 years). Amortization of leasehold improvements is provided on the straight-line method over the remaining minimum lease term.

*(e) Investment in ICOS - TBC*

The Company accounts for the investment in ICOS-TBC using the equity method. Because the Company had no basis in the technology transferred to ICOS-TBC as the Company's original investment, the Company did not record an amount for its original investment. The Company records its share of the ICOS-TBC loss as a liability to related party until the Company funds its portion of the loss.

ICOS-TBC paid a license fee and a milestone payment to the Company in 2000 and 2001, respectively. Because the Company has continuing obligations to ICOS-TBC, the Company deferred these amounts and is amortizing them into revenue over the estimated developmental period of the underlying technology.

*(f) Research and Development Costs*

All research and development costs are expensed as incurred and include salaries of research and development employees, certain rent and related building services, research supplies and services, clinical trial expenses and other

# TEXAS BIOTECHNOLOGY CORPORATION AND SUBSIDIARIES

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

associated costs. With respect to research and development, salaries and benefits for the years ended December 31, 2002, 2001 and 2000, of approximately \$9,283,000, \$7,296,000 and \$5,902,000, respectively, were charged to research and development. Payments related to the acquisition of in-process research and development, if any, are expensed as incurred.

*(g) Net Loss Per Common Share*

Basic net loss per common share is calculated by dividing the net loss applicable to common shares by the weighted average number of common and common equivalent shares outstanding during the period. For the years 2002, 2001 and 2000, there were no potential common equivalent shares used in the calculation of weighted average common shares outstanding.

	Year Ended December 31,		
	2002	2001	2000
Weighted average shares used to compute basic and diluted net loss per common share	43,741,258	43,636,548	39,149,882
Securities convertible into common stock, not used because the effect would be antidilutive:			
Stock options	5,012,500	4,131,252	3,152,316
Warrants	246,586	247,858	2,772,371
Total	5,259,086	4,379,110	5,924,687

*(h) Revenue Recognition*

Revenue from service contracts is recognized as services are performed. Royalty revenue is recognized as products are sold by a licensee and we have received sufficient information to record a receivable. The Company defers the recognition of milestone payments related to contractual agreements which are still in the development stage. Such deferred revenues are amortized into income over the estimated remaining development period. Milestone payments received under contractual agreements which have completed the development stage are evaluated, and either recognized into income when earned, or amortized over a future period, depending upon whether the Company continues to have obligations under the terms of the arrangement. License fees received under the terms of licensing agreements for the Company's intellectual property are similarly deferred, and amortized into income over the estimated development period of the licensed item or items. The Company periodically evaluates its estimates of remaining development periods, and adjusts the recognition of remaining deferred revenues over the adjusted development period remaining. Revenue from grants is recognized as earned under the terms of the related grant agreements, typically as expenses are incurred. Amounts received in advance of services being performed under contracts are recorded as deferred revenue, and recognized as services are performed.

*(i) Patent Application Costs*

Costs incurred in filing for, defending and maintaining patents are expensed as incurred.

*(j) Use of Estimates*

Management of the Company has made a number of estimates and assumptions relating to the reporting of assets and liabilities, revenues and expenses and the disclosure of contingent assets and liabilities to prepare these consolidated financial statements in conformity with accounting principles generally accepted in the United States of America. Actual results could differ from these estimates.

*(k) Intangible Assets*

Intangible assets, consisting of amounts paid for products approved by the United States Food and Drug Administration ("FDA"), are amortized on a straight-line basis over their estimated useful lives. The Company periodically reviews the useful lives of its intangible and long-lived assets, which may result in future adjustments to the amortization periods.

# TEXAS BIOTECHNOLOGY CORPORATION AND SUBSIDIARIES

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

Related amortization expense for the years ended December 31, 2002, 2001 and 2000 was \$106,000, \$106,000 and \$53,000, respectively. Amortization of intangible assets is included in general and administrative expense in the consolidated statements of operations and comprehensive loss.

*(l) Treasury Stock*

Treasury stock is recorded at cost. On May 3, 2001, the Company announced that its Board of Directors had authorized a stock repurchase program to buy up to 3 million shares, or approximately 7 percent of the Company's outstanding Common Stock over an 18 month period. Pursuant to the stock repurchase program, the Company repurchased 213,000 shares for net proceeds of approximately \$1,602,000 during the year ended December 31, 2001. No shares were repurchased during the year ended December 31, 2002.

*(m) Stock Based Compensation*

At December 31, 2002, the Company has six stock-based compensation plans for employees and non-employee directors, which are described more fully in Note 3. The Company accounts for those plans under the recognition and measurement principles of APB Opinion No. 25, *Accounting for Stock Issued to Employees*, and related interpretations. Net loss in the years ended December 31, 2002 and 2001 included stock-based compensation expense as a result of modifications made to certain options previously issued to retiring employees. Net loss in the year ended December 31, 2002 also includes stock-based compensation expense related to the grant of shares of restricted stock to the Company's CEO. No other stock-based employee compensation expense is reflected in net loss, however, as all options granted under those plans had an exercise price equal to the market price of the underlying common stock on the date of grant. The following table illustrates the effect on net loss and loss per share if the Company had applied the fair value recognition provisions of FASB Statement of Financial Accounting Standards No. 123, "Accounting for Stock-Based Compensation," (SFAS123) to stock-based employee compensation (\$ in thousands, except for per share data).

	Year Ended December 31,		
	2002	2001	2000
Net loss, as reported	\$ (23,469)	\$ (19,142)	\$ (5,655)
Add: Stock-based employee compensation expense included in reported net income	252	63	---
Deduct: Total stock-based employee compensation expense determined under fair value method for all awards	(4,238)	(4,118)	(2,950)
Pro forma net loss	\$ (27,455)	\$ (23,197)	\$ (8,605)
Loss per share:			
As reported, basic and diluted	<u>\$ (0.54)</u>	<u>\$ (0.44)</u>	<u>\$ (0.14)</u>
Pro forma, basic and diluted	<u>\$ (0.63)</u>	<u>\$ (0.53)</u>	<u>\$ (0.22)</u>

# TEXAS BIOTECHNOLOGY CORPORATION AND SUBSIDIARIES

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

The per-share weighted average fair value of stock options granted during 2002, 2001 and 2000 was \$3.45, \$3.62 and \$12.26, respectively, on the grant date using the Black-Scholes option pricing model with the following assumptions:

	Year Ended December 31,		
	2002	2001	2000
Expected dividend yield	0.0%	0.0%	0.0%
Risk-free interest rate	2.8%	4.2%	5.0%
Expected volatility	74.3%	78.0%	77.0%
Expected life in years	4.54	4.83	4.61

*(n) Income Taxes*

The Company uses the asset and liability method of accounting for income taxes. Under the asset and liability method, deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and operating loss and tax credit carryforwards.

Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date.

*(o) Impairment of Long-lived Assets*

As circumstances dictate, the Company evaluates the recoverability of its long-lived tangible and intangible assets by comparing the projected undiscounted net cash flows associated with such assets against their respective carrying values. Impairment, if any, is based on the excess of the carrying value over the fair value.

*(p) New Accounting Pronouncements*

In August 2001, the FASB issued Statement of Financial Accounting Standards No. 143, "Accounting for Asset Retirement Obligations," (SFAS143) which addresses financial accounting and reporting for obligations associated with the retirement of tangible long-lived assets and the associated asset retirement costs. This statement applies to all entities that have legal obligations associated with the retirement of long-lived assets that result from the acquisition, construction, development or normal use of the assets. SFAS143 is effective for all fiscal years beginning after June 15, 2002. The Company does not expect the adoption of SFAS143 to have a significant impact on its financial condition or results of operations.

In April 2002, the FASB issued Statement of Financial Accounting Standards No. 145, "Rescission of FASB Statements No. 4, 44 and 64, Amendment of FASB Statements No. 13 and Technical Corrections," (SFAS145). SFAS145 provides guidance for income statement classification of gains and losses on extinguishments of debt and accounting for certain lease modifications that have economic effects that are similar to sale-leaseback transactions. SFAS145 is effective for the Company in January 2003. The Company does not expect the adoption of SFAS145 to have a significant impact on its financial condition or results of operations.

In July 2002, the FASB issued Statement of Financial Accounting Standards No. 146, "Accounting for Costs Associated With Exit or Disposal Activities," (SFAS146) which addresses significant issues regarding the recognition, measurement and reporting of costs that are associated with exit and disposal activities, including restructuring activities that are currently accounted for pursuant to the guidance set forth in EITF Issue No. 94-3, "Liability Recognition of Certain Employee Termination Benefits and Other Costs to Exit an Activity." SFAS146 is effective for the Company in January 2003. The Company does not expect the adoption of SFAS146 to have a significant impact on its financial condition or results of operations.

# TEXAS BIOTECHNOLOGY CORPORATION AND SUBSIDIARIES

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

In December 2002, the FASB issued Statement of Financial Accounting Standards No. 148, "Accounting for Stock-Based Compensation—Transition and Disclosure," (SFAS148). SFAS148 amends SFAS123 to provide alternative methods of transition for a voluntary change to the fair value based method of accounting for stock-based employee compensation. In addition, SFAS148 amends the disclosure requirements of SFAS123 to require prominent disclosure in both annual and interim financial statements about the method of accounting for stock-based employee compensation and the effect of the method used on reported results. The provisions of SFAS148 are effective for fiscal years ending after December 15, 2002. The adoption of SFAS148 did not have a material impact on the consolidated financial statements.

### (q) Reclassifications

Certain reclassifications have been made to prior period financial statements to conform with the December 31, 2002 presentation with no effect on net loss previously reported.

### (2) Capital Stock

In December 1993, the Company completed an initial public offering comprised of 4,082,500 units, each unit consisting of one share of Common Stock (par value \$.005 per share) and one warrant to purchase one share of Common Stock. Proceeds to the Company were approximately \$24.2 million, net of selling expenses of approximately \$3.3 million. The securities included in the unit subsequently separated into its Common Stock and warrant components. The warrants were exercisable at \$8.44 per share. On December 13, 1998, the expiration date of the warrants was extended from December 14, 1998 to September 30, 1999 for those warrant holders electing such extension. On September 13, 1999, the expiration date of the warrants was further extended to December 31, 2000. There were 2,386,645 warrants outstanding as of December 31, 2000 which were exercised on January 3, 2001 for proceeds of approximately \$20.1 million.

In April 2000, the Company sold 5,584,591 shares of Common Stock for \$12.50 per share in an underwritten public offering. The net proceeds to the Company from this offering were approximately \$65.2 million after deducting selling commissions and expenses of approximately \$4.6 million related to the offering.

The Company has reserved Common Stock for issuance as of December 31, 2002 as follows:

Stock option plans .....	5,758,413
Warrants outstanding .....	<u>246,586</u>
Total shares reserved .....	<u>6,004,999</u>

### Shareholders' Rights Plan

In January 2002, the Company adopted a shareholder rights plan under which the Board of Directors declared a dividend of one preferred stock purchase right ("Right") for each outstanding share of the Company's common stock held of record as of the close of business on January 22, 2002. Each Right initially entitles a shareholder to purchase a one one-thousandth fraction of a share of Preferred Stock - Junior Participating Series A (the "Preferred Stock") for \$55.00. Each such fraction of a share of Preferred Stock has terms designed to make it essentially equivalent to one share of Common Stock. The Rights will become exercisable only in the event a person or group acquires 15% or more of the Company's Common Stock or commences a tender or exchange offer which, if consummated, would result in that person or group owning 15% of the Common Stock. Prior to such an event, the Rights will be evidenced by and traded in tandem with the Common Stock.

If a person or group acquires a 15% or larger position in the Company, each Right (except those held by the acquiring party) will then entitle its holder to purchase, fractional shares of Preferred Stock having twice the value of the \$55 exercise price, with each fractional Preferred Share valued at the market price of the Common Stock. Also, if following an acquisition of 15% or more of the Company's Common Stock, the Company is acquired by that person or group in a merger or other business combination transaction, each Right would then entitle its holder to purchase Common Stock of the acquiring company having a value of twice the \$55.00 exercise price. The effect will be to entitle the Company's shareholders to buy stock in the acquiring company at 50% of its market price.



# TEXAS BIOTECHNOLOGY CORPORATION AND SUBSIDIARIES

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

The Company may redeem the Rights at \$.001 per Right at any time on or prior to the tenth business day following the acquisition of 15% or more of its Common Stock by a person or group or commencement of a tender offer for such 15% ownership. The Rights expire on January 2, 2012.

### (3) Stock Options and Warrants

The Company has in effect the following stock option plans:

The Amended and Restated 1990 Incentive Stock Option Plan ("1990 Plan") allows for the issuance of incentive and non-qualified options to employees, directors, officers, non-employee independent contractors and non-employee directors, pursuant to which 102,635 shares of Common Stock are reserved for issuance out of authorized but unissued shares of the Company.

The Amended and Restated 1992 Incentive Stock Option Plan ("1992 Plan") allows for the issuance of incentive and non-qualified options to employees, directors, officers, non-employee independent contractors and non-employee directors, pursuant to which 712,641 shares of Common Stock are reserved for issuance out of authorized but unissued shares of the Company.

The Amended and Restated Stock Option Plan for Non-Employee Directors ("Director Plan") allows for the issuance of non-qualified options to non-employee directors, pursuant to which 28,527 shares of Common Stock are reserved for issuance out of authorized but unissued shares of the Company to be issued to non-employee members of the Board of Directors of the Company based on a formula. No new issuances are being made under the Director Plan.

The Amended and Restated 1995 Stock Option Plan ("1995 Plan") allows for the issuance of incentive and non-qualified options, shares of restricted stock and stock bonuses to employees, officers, and non-employee independent contractors, pursuant to which 1,604,867 shares of Common Stock are reserved for issuance out of authorized but unissued shares of the Company.

The Amended and Restated 1995 Non-Employee Director Stock Option Plan ("1995 Director Plan") allows for the issuance of non-qualified options to non-employee directors, pursuant to which 444,368 shares of Common Stock are reserved for issuance out of authorized but unissued shares of the Company to be issued to non-employee members of the Board of Directors of the Company based on a formula. During 2003, the Board of Directors amended the 1995 Director Plan to allow a total of 800,000 shares of Common Stock to be reserved for issuance. The amendment is subject to approval of the stockholders at the Company's annual meeting in 2003.

The Amended and Restated 1999 Stock Incentive Plan ("1999 Plan") allows for the issuance of incentive and non-qualified options, shares of restricted stock and stock bonuses to directors, employees, officers and non-employee independent contractors, pursuant to which 2,865,375 shares of Common Stock are reserved for issuance out of authorized but unissued shares of the Company. During 2003, the Board of Directors amended the 1999 Plan to allow a total of 4,750,000 shares of Common Stock to be reserved for issuance. The amendment is subject to approval of the stockholders at the Company's annual meeting in 2003.

**TEXAS BIOTECHNOLOGY CORPORATION AND SUBSIDIARIES**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

A summary of stock options as of December 31, 2002, follows:

<u>Stock Option Plans</u>	<u>Exercise Price Per Share</u>	<u>Authorized</u>	<u>Outstanding</u>	<u>Exercised/ Other</u>	<u>Exercisable</u>	<u>Available for Grant</u>
1990 Plan.....	\$1.38-\$21.59	285,715	102,635	183,080	86,805	---
1992 Plan.....	\$1.41-\$21.59	1,700,000	712,641	987,359	688,566	---
Director Plan.....	\$3.50-\$ 4.54	71,429	28,527	42,902	28,527	---
1995 Plan.....	\$1.31-\$21.59	2,000,000	1,574,841	395,133	1,496,272	30,026
1995 Director Plan...	\$1.38-\$11.31	500,000	386,596	55,632	324,096	57,772
1999 Plan.....	\$2.29-\$20.13	<u>3,000,000</u>	<u>2,207,260</u>	<u>134,625</u>	<u>504,085</u>	<u>658,115</u>
TOTALS.....		<u>7,557,144</u>	<u>5,012,500</u>	<u>1,798,731</u>	<u>3,128,351</u>	<u>745,913</u>

A summary of the status of the Company's stock option plans as of December 31, 2002, 2001 and 2000 and the changes during the years then ended is presented below:

	<u>Options</u>	<u>Weighted-Average Exercise Price</u>
Outstanding at January 1, 2000.....	3,224,219	\$4.53
Granted.....	624,160	18.66
Canceled.....	(77,159)	9.13
Exercised.....	<u>(618,904)</u>	3.75
Outstanding at December 31, 2000.....	3,152,316	7.36
Granted.....	1,042,700	5.69
Canceled.....	(51,496)	13.77
Exercised.....	<u>(12,268)</u>	4.15
Outstanding at December 31, 2001.....	4,131,252	6.87
Granted.....	1,272,225	5.74
Canceled.....	(261,117)	5.97
Exercised.....	<u>(129,860)</u>	3.50
Outstanding at December 31, 2002.....	<u>5,012,500</u>	\$6.72

In 2002 and 2001, the Company issued 99,734 shares at a weighted average market price of \$5.61 per share, and 51,051 shares at a weighted average market price of \$9.69 per share, of restricted Common Stock, respectively, as compensation to certain of its employees, which will vest over the three year period subsequent to its issuance. In 2002, 5,063 shares of previously issued restricted Common Stock were cancelled, as a result of the termination of employment of the grantees before such shares had vested.

**TEXAS BIOTECHNOLOGY CORPORATION AND SUBSIDIARIES**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

The following tables summarize information about the Company's stock options outstanding as of December 31, 2002, 2001 and 2000, respectively:

<u>Option Exercise Price</u>	<u>Options Outstanding as of 12/31/2002</u>	<u>Weighted Average Remaining Contractual Life</u>	<u>Weighted Average Exercise Price</u>	<u>Options Exercisable as of 12/31/2002</u>	<u>Weighted Average Exercise Price of Exercisable</u>
\$ 1.31 - \$ 4.53	1,261,140	3.74	\$ 3.53	1,195,140	\$ 3.53
\$ 4.54 - \$ 5.63	1,749,644	6.24	\$ 5.49	647,472	\$ 5.37
\$ 5.64 - \$ 7.19	1,400,222	5.93	\$ 6.41	845,222	\$ 6.56
\$ 7.20 - \$21.59	<u>601,494</u>	6.69	\$ 17.68	<u>440,517</u>	\$ 17.45
\$ 1.31 - \$21.59	<u>5,012,500</u>	5.58	\$ 6.72	<u>3,128,351</u>	\$ 6.69

<u>Option Exercise Price</u>	<u>Options Outstanding as of 12/31/2001</u>	<u>Weighted Average Remaining Contractual Life</u>	<u>Weighted Average Exercise Price</u>	<u>Options Exercisable as of 12/31/2001</u>	<u>Weighted Average Exercise Price of Exercisable</u>
\$ 1.31 - \$ 4.19	1,050,454	3.68	\$ 3.21	951,041	\$ 3.11
\$ 4.20 - \$ 5.51	1,526,834	6.44	\$ 5.17	734,486	\$ 4.80
\$ 5.52 - \$11.31	1,035,970	6.07	\$ 6.85	909,478	\$ 6.79
\$11.32 - \$21.59	<u>517,994</u>	8.02	\$ 19.36	<u>194,418</u>	\$ 19.37
\$ 1.31 - \$21.59	<u>4,131,252</u>	5.84	\$ 6.87	<u>2,789,423</u>	\$ 5.89

<u>Option Exercise Price</u>	<u>Options Outstanding as of 12/31/2000</u>	<u>Weighted Average Remaining Contractual Life</u>	<u>Weighted Average Exercise Price</u>	<u>Options Exercisable as of 12/31/2000</u>	<u>Weighted Average Exercise Price of Exercisable</u>
\$ 1.31 - \$ 3.50	638,719	2.86	\$ 2.64	637,886	\$ 2.64
\$ 3.51 - \$ 5.88	1,459,624	6.09	\$ 4.83	1,208,453	\$ 4.98
\$ 5.89 - \$ 8.13	451,146	7.17	\$ 7.19	297,282	\$ 7.19
\$ 8.14 - \$21.59	<u>602,827</u>	9.36	\$ 18.63	<u>23,752</u>	\$ 13.86
\$ 1.31 - \$21.59	<u>3,152,316</u>	5.84	\$ 7.36	<u>2,167,373</u>	\$ 4.69

**TEXAS BIOTECHNOLOGY CORPORATION AND SUBSIDIARIES**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

*Warrants*

A summary of the status of the Company's warrants as of December 31, 2002, 2001 and 2000, and changes during the years then ended is presented below:

	<u>Warrants</u>	<u>Weighted-Average Exercise Price</u>
Outstanding at January 1, 2000.....	4,760,972	\$8.01
Canceled.....	(1,457,473)	8.37
Exercised.....	<u>(531,128)</u>	4.76
Outstanding at December 31, 2000.....	2,772,371	8.33
Forfeited.....	(12,955)	4.40
Exercised.....	<u>(2,511,558)</u>	8.20
Outstanding at December 31, 2001.....	247,858	9.87
Exercised.....	<u>(1,272)</u>	4.25
Outstanding at December 31, 2002.....	<u>246,586</u>	\$9.90

On November 12, 1998, the Company announced an extension of the exercise period of the Company's publicly traded redeemable common stock purchase warrants from December 14, 1998 to September 30, 1999 for those warrant holders electing such extension. On September 13, 1999, the expiration date of the warrants was further extended to December 31, 2000. These publicly traded warrants comprised 2,386,645 of the 2,772,371 warrants outstanding at December 31, 2000. The exercise price of \$8.44 remained unchanged. On January 3, 2001, publicly traded warrants to purchase 2,386,645 shares were exercised and the Company received cash proceeds of \$20,143,000. In February 2001, warrants to purchase 124,913 shares at a weighted-average exercise price of \$3.60, originally issued in 1996, were exercised for total cash proceeds of \$450,000.

(4) **Income Taxes**

The Company did not incur any tax expense in any year due to operating losses and the related increase in the valuation allowance.

The reconciliation of income taxes at the statutory rate of 35% applied to income before taxes is as follows (\$ in thousands):

	<u>2002</u>	<u>December 31, 2001</u>	<u>2000</u>
Computed "expected" tax expense	\$ (8,214)	\$ (6,700)	\$ (1,979)
Effect of:			
Permanent differences	893	525	(2,020)
Increase in valuation allowance	<u>7,321</u>	<u>6,175</u>	<u>3,999</u>
Tax expense	<u>\$ ---</u>	<u>\$ ---</u>	<u>\$ ---</u>

**TEXAS BIOTECHNOLOGY CORPORATION AND SUBSIDIARIES**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

The tax effects of the temporary differences that give rise to significant portions of the deferred tax assets as of December 31, 2002 and 2001 are as follows (\$ in thousands):

	December 31,	
	2002	2001
Loss carryforwards	\$ 41,946	\$ 30,726
Start-up costs	8,001	10,748
Property, plant and equipment	(71)	814
Deferred revenue	2,053	2,393
Other	1,047	974
Gross deferred tax assets	52,976	45,655
Valuation allowance	(52,976)	(45,655)
Net deferred tax assets	<u>\$ ---</u>	<u>\$ ---</u>

The Company has established a valuation allowance for the full amount of these deferred tax assets, as management does not believe that it is more likely than not that the Company will recover these assets. Utilization of the Company's net operating loss carryforwards is subject to certain limitations due to specific stock ownership changes which have occurred or may occur. To the extent not utilized, the carryforwards will expire during the years beginning 2005 through 2022.

**(5) Equipment and Leasehold Improvements**

Equipment and leasehold improvements consist of the following (\$ in thousands):

	December 31,	
	2002	2001
Laboratory and office equipment.....	\$ 10,667	\$ 8,407
Leasehold improvements .....	4,311	4,302
	14,978	12,709
Less accumulated depreciation and amortization .....	9,399	8,409
	<u>\$ 5,579</u>	<u>\$ 4,300</u>

**(6) Entity-Wide Geographic Data**

The Company operates in a single business segment that includes research and development of pharmaceutical products. The following table summarizes the Company's long-lived assets in different geographic locations (\$ in thousands):

	December 31,	
	2002	2001
Long-lived assets:		
United States	\$ 4,884	\$ 4,446
Germany	1,457	722
Total	<u>\$ 6,341</u>	<u>\$ 5,168</u>

**(7) Research Agreements**

On October 10, 1996, the Company signed a strategic alliance agreement with LG Chemical, a Korean corporation, to develop and market compounds derived from the Company's endothelin receptor antagonist and selectin antagonist programs for certain disease indications. Upon consummation of the transaction, LG Chemical purchased 1,250,000 shares of Common Stock for \$4.00 per share for a total of \$5 million. In addition, LG Chemical had committed to pay \$10.7 million in research payments. Of this amount, \$8.1 million had been paid as of December 31, 2000. Effective June 6, 2000, the Company assigned one-half of the research payment to ICOS-TBC which amounted to \$577,000, before commissions, during the year 2000. In August 2001, the Company and LG Chemical mutually agreed to terminate the strategic alliance agreement. No research payments were received in 2002 or 2001 from LG Chemical and LG Chemical's rights under the agreement have ended.

# TEXAS BIOTECHNOLOGY CORPORATION AND SUBSIDIARIES

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

Under the terms of the Company's agreement with ICOS-TBC, the Company will provide, and be reimbursed for, research and development activities conducted on behalf of ICOS-TBC. In January 2003, ICOS announced that it had reached a conclusion that joint development of the endothelin antagonist program by ICOS-TBC should not continue. ICOS and TBC are currently negotiating the terms pursuant to which TBC could independently continue the program. The financial terms of the transaction are subject to ongoing negotiations between the two companies. See Note 8, below.

The Company also receives reimbursement for certain research costs pursuant to its agreements with GlaxoSmithKline, plc ("GSK") (Note 10), Schering-Plough LTD. and Schering-Plough Corporation (collectively "Schering-Plough") (Note 8) and Revotar (Note 9).

### (8) License Agreements

#### *Mitsubishi-Pharma Agreement*

TBC has entered into an agreement with Mitsubishi Pharma Corporation, formerly Mitsubishi-Tokyo Pharmaceuticals, Inc. ("Mitsubishi") to license Mitsubishi's rights and technology relating to Argatroban and to license Mitsubishi's own proprietary technology developed with respect to Argatroban (the "Mitsubishi Agreement"). Under the Mitsubishi Agreement, the Company has an exclusive license to use and sell Argatroban in the U.S. and Canada for all specified indications. The Company is required to pay Mitsubishi specified royalties on net sales of Argatroban by the Company and its sublicensees after its commercial introduction in the U.S. and Canada. Either party may terminate the Mitsubishi Agreement on 60 days notice if the other party defaults in its material obligations under the agreement, declares bankruptcy or is insolvent, or if a substantial portion of its property is subject to levy. Unless terminated sooner pursuant to the above described termination provisions, the Mitsubishi Agreement expires on the later of termination of patent rights in a particular country or 20 years after first commercial sale of products. Under the Mitsubishi Agreement, TBC has access to an improved formulation patent granted in 1993 which expires in 2010 and a use patent which expires in 2009. The Mitsubishi composition of matter patent on Argatroban has expired. During 2000, TBC signed an additional agreement with Mitsubishi that provides TBC with royalties on sales of Argatroban in certain European countries, up to a total of \$5.0 million in milestones for the development of ischemic stroke and certain other provisions. The Company began enrolling patients in a clinical trial for ischemic stroke in April 2001, and received a \$2.0 million milestone payment in May 2001, which is being recognized as revenues over the expected development period, and accordingly, revenues in years 2002 and 2001 include approximately \$382,000 and \$274,000, respectively, related to such milestone payment. In light of a lack of a positive overall efficacy trend and the high risk and high costs associated with stroke trials, it is unlikely that we will proceed independently with a full Phase III program. In conjunction with the Mitsubishi Agreement, a consulting firm involved in negotiations related to the agreement will receive a percentage of net sales received as a result of the agreement.

Mitsubishi further agreed to supply the Company with its requirements of bulk Argatroban throughout the term of the Mitsubishi Agreement for TBC's clinical testing and commercial sales of Argatroban in the U.S. and Canada. In the event Mitsubishi should discontinue the manufacture of Argatroban, Mitsubishi and TBC have agreed to discuss in good faith the means by which, and the party to whom, Argatroban production technology will be transferred. The transferee may be a person or entity other than TBC. At present, Mitsubishi is the only manufacturer of Argatroban. See Note 10.

In exchange for the license to the Genentech, Inc. (the "Former Licensor") Argatroban technology, TBC issued the Former Licensor 285,714 shares of Common Stock during 1993 and issued an additional 214,286 shares of Common Stock on October 9, 1997, after acceptance of the filing of the first New Drug Application ("NDA") with the United States Food and Drug Administration (the "FDA") for Argatroban. On June 30, 2000, the Company issued an additional 71,429 shares of Common Stock to Genentech in conjunction with the approval of the NDA for Argatroban in patients with HIT. The value of \$965,000 has been recorded as an intangible asset and is being amortized over the estimated useful life of the asset. Amortization expense recorded in 2002, 2001 and 2000 was \$105,000, \$105,000 and \$53,000, respectively and will be approximately \$105,000 annually in future periods. Additionally, on October 9, 1997, upon acceptance of the filing of the first NDA for Argatroban with the FDA, the Company granted the Former Licensor a warrant to purchase an additional 142,858 shares of Common Stock at an exercise price of \$14.00 per share, subject to adjustment, which expires on October 9, 2004. TBC has also granted the Former Licensor demand and piggyback registration rights with regard to shares of Common Stock issued to the Former Licensor.

**TEXAS BIOTECHNOLOGY CORPORATION AND SUBSIDIARIES**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

During the third quarter of 1997, the Company sublicensed certain rights to Argatroban to GSK. In conjunction with this agreement, the Company agreed to make certain payments to Mitsubishi, which are included in research and development expense, to pay an additional royalty to Mitsubishi, beginning January 1, 2002 and to provide access to certain Argatroban clinical data to Mitsubishi in certain circumstances. In certain circumstances, Mitsubishi and TBC will share equally in all upfront payments and royalties should Mitsubishi use TBC's regulatory documents and data for registration in certain territories. See Note 10.

*ICOS Corporation Partnership*

On June 6, 2000, the Company and ICOS entered into the ICOS-TBC limited partnership agreement. The partnership was established to develop and globally commercialize ET<sub>A</sub> receptor antagonists. As a result of its contribution of technology, ICOS-TBC paid a license fee to TBC in June 2000. In July 2001, the Company earned a milestone, as a result of the achievement of an objective defined in the partnership agreement. The license fee is being amortized over the estimated development period of the licensed technology and the Company recognized approximately \$464,000, \$484,000 and \$307,000 of it as revenue during 2002, 2001 and 2000, respectively. The milestone payment received in July 2001 is also being amortized over the estimated development period, and the Company recognized approximately \$640,000 and \$333,000 of it as revenue during 2002 and 2001, respectively. For further discussion of the Company's revenue recognition policies, see Note 1 (h), Revenue Recognition, above. In January 2003, ICOS announced that it had reached a conclusion that joint development of the endothelin antagonist program by ICOS-TBC should not continue. ICOS and TBC are currently negotiating the terms pursuant to which TBC could independently continue the program. The financial terms of the transaction are subject to ongoing negotiations between the two companies. After December 31, 2002, TBC has agreed to be responsible for 100% of the expenses of ICOS-TBC.

During the years ended December 31, 2002, 2001 and 2000, the Company recognized losses of \$8,557,000, \$9,450,000 and \$3,487,000, respectively, representing the Company's proportionate share of the losses of ICOS-TBC. The losses of ICOS-TBC includes amounts billed to the partnership by the Company, all of which were included in the loss of the partnership, as follows (\$ in thousands):

	<u>Year Ended December 31,</u>		
	<u>2002</u>	<u>2001</u>	<u>2000</u>
Charges for TBC labor costs	\$ 1,090	\$ 1,442	\$ 1,123
Direct research and development costs	1,375	4,748	3,583
Total billed to ICOS-TBC by the Company	<u>\$ 2,465</u>	<u>\$ 6,190</u>	<u>\$ 4,706</u>

Summarized unaudited financial information for ICOS-TBC is as follows (\$ in thousands):

**Financial position - December 31:**

	<u>2002</u>	<u>2001</u>
Total assets - all current .....	<u>\$ 1</u>	<u>\$ 1</u>
Total liabilities - all current, payable to partners.....	\$ 5,235	\$ 7,059
Partners' deficit.....	<u>(5,234)</u>	<u>(7,058)</u>
	<u>\$ 1</u>	<u>\$ 1</u>

<u>Operating results:</u>	<u>Year ended</u>	<u>Year ended</u>	<u>Period from</u>
	<u>December 31,</u>	<u>December 31,</u>	<u>June 6, 2000</u>
	<u>2002</u>	<u>2001</u>	<u>(inception)</u>
			<u>through</u>
			<u>December 31,</u>
			<u>2000</u>
Revenue .....	\$ ---	\$ ---	\$ 547
Research and development expenses, related parties....	(16,633)	(18,872)	(7,515)
Contribution of technology, related party .....	---	(4,000)	(4,000)
Administrative expenses .....	<u>(483)</u>	<u>(26)</u>	<u>(8)</u>
Net loss .....	<u>\$(17,116)</u>	<u>\$(22,898)</u>	<u>\$ (10,976)</u>

# TEXAS BIOTECHNOLOGY CORPORATION AND SUBSIDIARIES

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

### *Schering-Plough Research Collaboration and License Agreement*

On June 30, 2000, TBC and Schering-Plough entered into a worldwide research collaboration and license agreement to discover, develop and commercialize VLA-4 antagonists. VLA-4 antagonists represent a new class of compounds that has shown promise in multiple preclinical animal models of asthma. The primary focus of the collaboration will be to discover orally available VLA-4 antagonists as treatments for asthma.

Under the terms of the agreement, Schering-Plough obtains the exclusive worldwide rights to develop, manufacture and market all compounds from TBC's library of VLA-4 antagonists, as well as the rights to a second integrin antagonist. TBC will be responsible for optimizing a lead compound and additional follow-on compounds. Schering-Plough is supporting research at TBC and will be responsible for all costs associated with the worldwide product development program and commercialization of the compound. In addition to reimbursing research costs, Schering-Plough paid an upfront license fee and will pay development milestones and royalties on product sales resulting from the agreement. This upfront license fee is being amortized into revenue over the expected development period, and the Company recognized \$366,000, \$456,000 and \$273,000 of the license fee as revenues in years 2002, 2001 and 2000, respectively. Total payments to TBC for both programs, excluding royalties, could reach \$87.0 million.

In June 2002, the Company achieved a milestone under the Schering-Plough agreement as a result of the nomination of an initial candidate for Schering-Plough's further development. This milestone payment will be recognized into revenue over the expected development period, and approximately \$104,000 was recognized as revenue during 2002.

### (9) Foreign Subsidiary

During the third quarter 2000, TBC formed Revotar to conduct research and development of novel small molecule compounds and to develop and commercialize selectin antagonists. Upon formation, Revotar received certain development and commercialization rights to the Company's selectin antagonist compounds as well as rights to certain other TBC research technology. Revotar also received approximately \$5 million in funding from three German venture capital funds. The Company retained ownership of approximately 55% of the outstanding common stock of Revotar and has consolidated the financial results of Revotar into TBC's consolidated financial statements. Since the development and commercialization rights contributed by the Company to Revotar had no basis for financial reporting purposes, the Company assigned no value to its contribution of intellectual property rights. The Company's equity in the originally contributed assets by the minority shareholders is included with the minority interest in Revotar on the consolidated balance sheets at December 31, 2002 and 2001. The minority interest in Revotar at December 31, 2002 and December 31, 2001, was \$2,608,000 and \$3,833,000, respectively. The Company's consolidated net loss for the years ended December 31, 2002, 2001 and 2000 was reduced \$1,225,000, \$749,000 and \$209,000, respectively, by the Revotar minority shareholders' approximately 45% interest in Revotar's losses.

### (10) Commercialization Agreement

In connection with TBC's development and commercialization of Argatroban, in August 1997, TBC entered into a Product Development, License and CoPromotion Agreement with GSK (the "GSK Agreement") whereby GSK was granted exclusive rights to work with TBC in the development and commercialization of Argatroban in the U.S. and Canada for specified indications. GSK paid \$8.5 million in upfront license fees during August 1997, a \$5 million milestone payment in October 1997, and a \$7.5 million milestone payment in June 2000. Additional milestone payments may be earned upon the clinical development and FDA approval for the acute myocardial infarction indication. Future milestone payments for the acute myocardial infarction indication are subject to GSK's agreement to market Argatroban for such indication. The parties have also formed a joint development committee to analyze the development of additional Argatroban indications to be funded 60% by GSK except for certain Phase IV trials which shall be funded entirely by GSK. At this time, GSK has no plans to conduct development work for the acute myocardial infarction and stroke indications. GSK has the exclusive right to commercialize all products arising out of the collaboration, subject to the obligation to pay royalties on net sales to TBC and to the rights of TBC to co-promote these products through its own sales force in certain circumstances. TBC will retain the rights to any indications which GSK determines it does not wish to pursue (such as ischemic stroke), subject to the requirement that TBC must use its own sales force to commercialize any such indications. Any indications which TBC elects not to pursue will be returned to Mitsubishi. In conjunction with the GSK Agreement, a consulting firm involved in negotiations related to the agreement will receive a percentage of all consideration received by TBC as a result of the agreement.



# TEXAS BIOTECHNOLOGY CORPORATION AND SUBSIDIARIES

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

At present, Mitsubishi is the only manufacturer of Argatroban, and has entered into the Mitsubishi Supply Agreement with GSK to supply Argatroban in bulk in order to meet GSK and TBC's needs under the GSK Agreement. Should Mitsubishi fail during any consecutive nine-month period to supply GSK at least 80% of its requirements, and such requirements cannot be satisfied by existing inventories, the Mitsubishi Supply Agreement provides for the nonexclusive transfer of the production technology to GSK. If GSK cannot commence manufacturing of Argatroban or alternate sources of supply are unavailable or uneconomic, the Company's results of operations would be materially and adversely affected.

The GSK Agreement generally terminates on a country by country basis upon the earlier of the termination of TBC's rights under the Mitsubishi Agreement, the expiration of applicable patent rights or, in the case of royalty payments, the commencement of substantial third-party competition. GSK also has the right to terminate the agreement on a country by country basis by giving TBC at least three months written notice at any time before GSK first markets products in that country based on a reasonable determination by GSK that the commercial profile of the product in question would not justify continued development in that country. GSK has similar rights to terminate the GSK Agreement on a country by country basis after marketing has commenced. In addition, either party may terminate the GSK Agreement on 60 days notice if the other party defaults in its obligations under the agreement, declares bankruptcy or is insolvent.

In connection with the execution of the GSK Agreement, GSK purchased 176,992 shares of TBC's Common Stock for \$1.0 million and additional 400,000 shares of Common Stock for \$2.0 million in connection with the secondary public offering, which closed on October 1, 1997.

### (11) 401(k) Plan

The Company adopted a 401(k) plan which became effective on September 1, 1993. Under the plan, all employees with three months of service are eligible to participate in the plan and may contribute up to 15 percent of their compensation, with a maximum of \$11,000 per employee in 2002. The Compensation Committee of the Board of Directors approved an employer matching contribution of \$0.50 on the dollar of employee contributions up to 6% of salaries and the 401(k) plan was amended effective January 1, 2001. The Compensation Committee approved matching contributions on the catch-up contribution made by employees 50 years of age or older by the end of the plan year and the 401(k) plan was amended effective January 1, 2002. Total cost of the employer match was \$197,000 and \$158,000 in 2002 and 2001, respectively.

### (12) Commitments and Contingencies

#### (a) Employment Agreements

The Company has entered into employment agreements with certain officers and key employees. Additionally, the Company has signed agreements with nine of its officers to provide certain benefits in the event of a "change of control" as defined in these agreements and the occurrence of certain other events. The agreements provide for a lump-sum payment in cash equal to eighteen months to three years of annual base salary and annual bonus, if any. The base salary and annual bonus portion of the agreements would aggregate approximately \$4.9 million at the current rate of compensation. In addition, the agreements provide for gross-up for certain taxes on the lump-sum payment, continuation of certain insurance and other benefits for periods of eighteen months to three years and reimbursement of certain legal expenses in conjunction with the agreements.

#### (b) Lease Agreements

In April 2002, the Company leased a facility in Bellaire, Texas, that houses the Company's administrative, marketing, clinical development and regulatory staff. Under the terms of the lease, which expires on July 31, 2005, the Company is obligated to pay approximately \$281,000 annually for base rent, related building services and parking. The Company has the right to extend the term of this lease agreement under the same terms and conditions to December 31, 2005, upon notice to the lessor. The Company could be subject to additional charges for related building services in years 2003 and thereafter, based upon increases in actual building costs, not to exceed six percent annually.

# TEXAS BIOTECHNOLOGY CORPORATION AND SUBSIDIARIES

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

The Company's lease on its laboratory facility in Houston, Texas expires on December 31, 2005 with an annual base rent of approximately \$815,000. The Company also leases parking spaces at the facility established rate charged, which currently approximates \$43,000 per year. The lease also includes a provision for the Company to pay certain additional charges to obtain utilities and building services during off-business hours. Currently, the amount of these charges is approximately \$288,000 per annum, payable in monthly installments. These charges are subject to annual adjustments based on the local consumer price index.

In October 2001, Revotar, the Company's majority-owned subsidiary, leased an 8,800 square foot office and laboratory facility in Berlin, Germany. The lease expires on September 30, 2006. Under the terms of the lease, the Company is obligated to pay \$137,000 in year 2003 for rent and parking. Under the terms of the lease, base rent will increase at three percent per year on the anniversary date of the lease. In addition to the base rent and parking, the Company is obligated to pay \$49,000 in year 2003 for related building services. The charge for related building services is subject to annual adjustments, based upon actual increases in costs, up to six percent per year.

For the years ended December 31, 2002, 2001 and 2000, rent and related building services totaled approximately \$1,600,000, \$1,200,000 and \$1,100,000, respectively.

At December 31, 2002, the Company's minimum aggregate commitments under long-term, non-cancelable operating leases are as follows (\$ in thousands):

2003.....	\$ 1,616
2004.....	1,620
2005.....	1,506
2006.....	131
	<u>\$ 4,873</u>

### (c) Foreign Currency Exchange Risk

The Company is exposed to market risk primarily from changes in foreign currency exchange rates.

The Company has a majority-owned subsidiary in Germany and consolidates the results of operations into its consolidated financial results. Although not significant to date, the Company's reported expenses and cash flows from this subsidiary are exposed to changing exchange rates. The Company had an intercompany receivable from our German subsidiary at December 31, 2002; however this amount was denominated in U.S. dollars and was not exposed to exchange risk. The Company contracts with entities in other areas outside the U.S. that are denominated in a foreign currency. To date, the currencies of these countries have not fluctuated materially. Through December 31, 2002, management has not deemed it cost effective to engage in a program of hedging the effect of foreign currency fluctuations on the Company's operating results using derivative financial instruments. During 2003, Revotar engaged in a program of hedging the effect of foreign currency fluctuations on approximately \$1.6 million in future loan payments from us.

### (d) Other Contingencies

Like other biopharmaceutical companies, the Company is subject to other contingencies, including legal proceedings and claims arising out of its business that cover a wide range of matters, including, among others, environmental matters, contract and employment claims, and product liability. The Company may be involved in legal actions from time to time. The Company has used various substances in its research and development which have been or may be deemed to be hazardous or dangerous, and the extent of its potential liability, if any, under environmental, product liability and workers' compensation statutes, rules, regulations and case law is unclear. The Company is not a party to any legal actions.

**TEXAS BIOTECHNOLOGY CORPORATION AND SUBSIDIARIES**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

**(13) Quarterly Financial Data (Unaudited)**

The following is a summary of the unaudited quarterly results of operations (in thousands, except per share data):

	Year Ended December 31, 2002			
	Quarter ended <u>March 31</u>	Quarter ended <u>June 30</u>	Quarter ended <u>September 30</u>	Quarter ended <u>December 31</u>
Total revenues	\$ 2,593	\$ 2,626	\$ 2,405	\$ 2,809
Operating loss	\$ (7,774)	\$ (7,057)	\$ (6,760)	\$ (5,575)
Net loss	<u>\$ (6,750)</u>	<u>\$ (6,221)</u>	<u>\$ (5,840)</u>	<u>\$ (4,658)</u>
Net loss per share data:				
Basic and diluted	\$ (0.15)	\$ (0.14)	\$ (0.13)	\$ (0.11)

	Year Ended December 31, 2001			
	Quarter ended <u>March 31</u>	Quarter ended <u>June 30</u>	Quarter ended <u>September 30</u>	Quarter ended <u>December 31</u>
Total revenues	\$ 2,269	\$ 2,463	\$ 1,704	\$ 2,481
Operating loss	\$ (4,224)	\$ (6,107)	\$ (5,707)	\$ (9,089)
Net loss	<u>\$ (2,510)</u>	<u>\$ (4,539)</u>	<u>\$ (4,289)</u>	<u>\$ (7,804)</u>
Net loss per share data:				
Basic and diluted	\$ (0.06)	\$ (0.10)	\$ (0.10)	\$ (0.18)

Because of the method used in calculating per share data, the quarterly per share data will not necessarily total to the per share data as computed for the year.

**(14) Subsequent Events**

In January 2003, the Company implemented a restructuring plan to reduce its annual fixed operating expenses. The Company eliminated approximately 21 positions, primarily in its research area, and cancelled approximately 15 open positions. The Company will incur a charge of approximately \$600,000 in 2003 related to the implementation of its restructuring plan.

On March 21, 2003, Nasdaq informed us that for the last 30 consecutive trading days, the bid price of our common stock has closed below the minimum \$1.00 per share requirement for continued inclusion in The Nasdaq National Market. Therefore, in accordance with Nasdaq Rules, we will be provided 180 calendar days, or until September 17, 2003, to regain compliance. If, at any time before September 17, 2003, the bid price of our common stock closes at \$1.00 per share or more for a minimum of 10 consecutive trading days, Nasdaq will provide written notification that we have achieved compliance with this rule. If compliance with this rule cannot be demonstrated by September 17, 2003, the Nasdaq will provide written notification that our securities will be delisted. At that time, we may appeal this determination to a Listing Qualifications Panel or may apply to transfer our securities to The Nasdaq Small Cap Market.

## INDEX TO EXHIBITS

<u>Exhibit No</u>	<u>Description of Exhibit</u>
3.1	— Certificate of Incorporation, as amended (incorporated by reference to Exhibit 3.1 to the Company's Form 10 (Commission File No. 0-20117) effective June 26, 1992 (as amended))
3.2	— Amendment to the Certificate of Incorporation dated November 30, 1993 (incorporated by reference to Exhibit 3.4 to the Company's Form 10-Q (Commission File No. 0-20117) filed with the Commission on November 14, 1994)
3.3	— Amendment to the Certificate of Incorporation dated May 20, 1994 (incorporated by reference to Exhibit 3.5 to the Company's Form 10-Q (Commission File No. 0-20117) filed with the Commission on November 14, 1994)
3.4	— Certificate of Amendment of Certificate of Incorporation dated May 3, 1996 (incorporated by reference to Exhibit 3.6 to the Company's Form 10-Q (Commission File No. 1-12574) for the quarter ended June 30, 1996)
3.5	— Amended and Restated By-laws of Texas Biotechnology Corporation adopted September 6, 1996 (incorporated by reference to Exhibit 3.7 to the Company's Form 10-Q (Commission File No. 1-12574) for the quarter ended September 30, 1996)
3.6	— Amendment to Article II of By-laws adopted June 29, 2000 (incorporated by reference to Exhibit 3.8 to the Company's Quarterly Report on Form 10-Q (Commission File No. 000-20117) for the quarter ended June 30, 2000 with the commission on August 14, 2000)
3.7	— Certificate of Designations, Preferences, Limitations and Relative Rights of The Series A Junior Participating Preferred Stock of Texas Biotechnology Corporation (incorporated by reference to Exhibit 2 to the Company's Form 8-A (Commission File No. 0-20117) with the commission on January 3, 2002)
4.1	— Rights Agreement, dated as of January 2, 2002, between Texas Biotechnology Corporation and The Bank of New York, as Rights Agent, including exhibits thereto. (incorporated by reference to Exhibit 1 to the Company's Form 8-A (Commission File No. 0-20117) with the commission on January 3, 2002)
4.2	— Form of Rights Certificate (incorporated by reference to Exhibit 3 to the Company's Form 8-A (Commission File No. 0-20117) with the commission on January 3, 2002)
10.1	— Consulting Agreement with John M. Pietruski dated January 1, 1992 (incorporated by reference to Exhibit 10.6 to the Company's Form 10 (Commission File No. 0-20117) effective June 26, 1992 (as amended))
10.2†	— Sixth amendment dated January 1, 2003 to Consulting Agreement with John M. Pietruski dated January 1, 1992.
10.3	— Employment Agreement with David B. McWilliams dated July 15, 1992 (incorporated by reference to Exhibit 19.1 to the Company's Form 10-Q (Commission File No. 0-20117) for the quarter ended June 30, 1992)
10.4	— Retirement Agreement between Texas Biotechnology Corporation and David B. McWilliams dated March 21, 2002 (incorporated by reference to Exhibit 10.28 to the Company's Form 10-K (Commission File No. 1-12574) for the year ended December 31, 2001 with the commission on March 29, 2002).
10.5†	— Termination Agreement between Texas Biotechnology Corporation and Bruce D. Given, M.D. dated March 21, 2003.
10.6†	— Termination Agreement between Texas Biotechnology Corporation and Richard A. F. Dixon dated March 17, 2003.
10.7†	— Termination Agreement between Texas Biotechnology Corporation and Stephen L. Mueller dated March 20, 2003.
10.8†	— Form of Termination Agreement between Texas Biotechnology Corporation and Tom Brock, Philip Brown, Heather Giles, Pam Mabry, Dan Thompson, and Patrick Ward.
10.9	— Form of Indemnification Agreement between Texas Biotechnology Corporation and its officers and directors dated March 12, 2002 (incorporated by reference to Exhibit 10.27 to the Company's Form 10-K (Commission File No. 1-12574) for the year ended December 31, 2001 with the commission on March 29, 2002).

- 10.10 — Amended and Restated 1990 Incentive Stock Option Plan (incorporated by reference to Exhibit 10.33 to the Company's Form 10-K (Commission File No. 0-20117) for the year ended December 31, 1994)
- 10.11 — Amended and Restated 1992 Incentive Stock Option Plan (as of March 3, 1995) (incorporated by reference to Exhibit 10.34 to the Company's Form 10-K (Commission File No. 0-20117) for the year ended December 31, 1994)
- 10.12 — Amended and Restated Stock Option Plan for Non-Employee Directors (incorporated by reference to Exhibit 10.39 to the Company's Form 10-Q (Commission File No. 0-20117) for the quarter ended June 30, 1995)
- 10.13 — 1995 Stock Option Plan (incorporated by reference to Exhibit 10.40 to the Company's Form 10-Q (Commission File No. 0-20117) for the quarter ended June 30, 1995)
- 10.14 — Amendment to the 1995 Stock Option Plan of Texas Biotechnology Corporation dated March 4, 1997 (incorporated by reference to Exhibit 10.62 to the Company's Form 10-Q (Commission File No. 1-12574) for the quarter ended June 30, 1997 with the Commission on August 14, 1997)
- 10.15 — Amended and Restated 1995 Non-Employee Director Stock Option Plan (as amended by the Board of Directors on June 30, 1996) (incorporated by reference to Exhibit 10.55 to the Company's Form 10-Q (Commission File No. 1-12574) for the quarter ended June 30, 1996)
- 10.16 — Amendment to the 1995 Non-Employee Director Stock Option Plan of Texas Biotechnology Corporation dated March 4, 1997 (incorporated by reference to Exhibit 10.63 to the Company's Form 10-Q (Commission File No. 1-12574) for the quarter ended June 30, 1997 with the Commission on August 14, 1997)
- 10.17 — Amendment to Amended and Restated 1995 Non-Employee Director Stock Option Plan, dated March 6, 2000 (incorporated by reference to Exhibit 4.1 to the Company's Registration Statement on Form S-8 (Commission File No. 333-41864) with the commission on July 20, 2000)
- 10.18 — Texas Biotechnology Corporation 1999 Stock Incentive Plan (incorporated by reference to Exhibit 10.71 to the Company's Form 10-Q (Commission File No. 1-12574) for the Quarter ended March 31, 1999 with the Commission on May 13, 1999)
- 10.19 — Amendment to the 1999 Stock Incentive Plan adopted on March 13, 2001 (incorporated by reference to Exhibit 4.1 to the Company's Registration Statement on Form S-8 (Commission File No. 333-72468) with the commission on October 30, 2001)
- 10.20 — Lease Agreement dated, February 24, 1995 between Texas Biotechnology Corporation and Doctors Center, Inc. (incorporated by reference to Exhibit 10.31 to the Company's Form 10-K (Commission File No. 0-20117) for the year ended December 31, 1994)
- 10.21† — Third Amendment to Lease Agreement dated January 1, 2003 between Texas Biotechnology Corporation and the Board of Regents of The University of Texas System.
- 10.22† — Lease Agreement dated February 20, 2002 between Texas Biotechnology Corporation and FRM West Loop Associates #6, LTD.
- 10.23\* — Sublicense and License Agreement dated May 27, 1993 between Company and Genentech, Inc., together with exhibits (incorporated by reference to Exhibit 10.17 to the Company's Form 10-Q (Commission File No. 0-20117) for the quarter ended June 30, 1993 and incorporated by reference to Exhibit 10.17 to the Company's Form 10-Q/A-1 (Commission File No. 0-20117) for the quarter ended June 30, 1993)
- 10.24\* — Stock Agreement dated May 27, 1993 between the Company and Genentech, Inc. (incorporated by reference to Exhibit 10.18 to the Company's Form 10-Q (Commission File No. 0-20117) for the quarter ended June 30, 1993)
- 10.25 — Agreement between Mitsubishi Chemical Corporation, Texas Biotechnology Corporation and SmithKline Beecham plc dated August 5, 1997 (incorporated by reference to Exhibit 99.1 to the Company's Form 8-K (Commission File No. 1-12574) with the Commission on August 25, 1997)
- 10.26\* — Product Development License and Co-Promotion Agreement between Texas Biotechnology Corporation and SmithKline Beecham plc dated August 5, 1997 (incorporated by reference to Exhibit 99.2 to the Company's Form 8-K (Commission File No. 1-12574) with the Commission on August 25, 1997)

- 10.27\* — Common Stock Purchase Agreement between Texas Biotechnology Corporation and SmithKline Beecham plc dated August 5, 1997 (incorporated by reference to Exhibit 99.3 to the Company's Form 8-K (Commission File No. 1-12574) with the Commission on August 25, 1997)
- 10.28\*† — Amended and Restated License and Research Development Agreement dated January 24, 2003 between Revotar Biopharmaceuticals AG and Texas Biotechnology Corporation.
- 10.29\* — Agreement of Limited Partnership of ICOS-Texas Biotechnology L.P. among ICOS-ET-LP LLC and Texas Biotechnology Corporation, as Limited Partners, and ICOS-ET-GP LLC and TBC-ET, Inc., as General Partners dated June 6, 2000. (incorporated by reference to Exhibit 99.4 to the Company's Quarterly Report on Form 10-Q (Commission File No. 000-20117) for the quarter ended June 30, 2000 with the commission on August 14, 2000)
- 10.30\* — Endothelin License Agreement by and between Texas Biotechnology Corporation and ICOS-Texas Biotechnology L.P. dated June 6, 2000. (incorporated by reference to Exhibit 99.5 to the Company's Quarterly Report on Form 10-Q (Commission File No. 000-20117) for the quarter ended June 30, 2000 with the commission on August 14, 2000)
- 10.31\* — Formation and Performance Agreement by and between ICOS Corporation and Texas Biotechnology Corporation dated June 6, 2000. (incorporated by reference to Exhibit 99.6 to the Company's Quarterly Report on Form 10-Q (Commission File No. 000-20117) for the quarter ended June 30, 2000 with the commission on August 14, 2000)
- 10.32\* — Research and Development Service Agreement by and between ICOS Corporation, Texas Biotechnology Corporation and ICOS-Texas Biotechnology L.P. dated June 6, 2000. (incorporated by reference to Exhibit 99.7 to the Company's Quarterly Report on Form 10-Q (Commission File No. 000-20117) for the quarter ended June 30, 2000 with the commission on August 14, 2000)
- 10.33\* — Research Collaboration and License Agreement by and between Texas Biotechnology Corporation and Schering-Plough LTD. dated June 30, 2000. (incorporated by reference to Exhibit 99.8 to the Company's Quarterly Report on Form 10-Q (Commission File No. 000-20117) for the quarter ended June 30, 2000 with the commission on August 14, 2000)
- 10.34\* — Research Collaboration and License Agreement by and between Texas Biotechnology Corporation and Schering Corporation dated June 30, 2000. (incorporated by reference to Exhibit 99.9 to the Company's Quarterly Report on Form 10-Q (Commission File No. 000-20117) for the quarter ended June 30, 2000 with the commission on August 14, 2000)
- 21.1† — Subsidiaries of the Registrant
- 23.1† — Independent Auditors' Consent of KPMG LLP, Seattle, Washington
- 23.2† — Independent Auditors' Consent of KPMG LLP, Houston, Texas
- 99.1† — Certification Pursuant to 18 U.S.C. Section 1350, As Adopted Pursuant To Section 906 of the Sarbanes-Oxley Act of 2002.
- 99.2† — Certification Pursuant to 18 U.S.C. Section 1350, As Adopted Pursuant To Section 906 of the Sarbanes-Oxley Act of 2002.

---

\* The Company has omitted certain portions of these agreements in reliance on Rule 24b-2 under the Securities and Exchange Act of 1934, as amended.

† Filed herewith