SANGSTAT MEDICAL CORP
Form 10-K
March 26, 2003

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

x **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

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

For the transition period from _____to _____

Commission File Number: 0-22890

SANGSTAT MEDICAL CORPORATION

(Exact name of registrant as specified in its charter)

Delaware	**94-3076-069**
(State or Other Jurisdiction of Incorporation or Organization)	**(IRS Employer Identification Number)**

6300 Dumbarton Circle Fremont, California 94555

(Address of principal executive offices, including zip code)

510-789-4300
(Registrant s telephone number, including area code)

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

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

Common Stock ($.001 par value)
Preferred Share 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
x	o

Indicate by a 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. o

Indicate by check mark whether the registrant is an accelerated filer (as defined in Rule 12b-2 of the Act)

Yes	No
x	o

The approximate aggregate market value of the Common Stock held by non-affiliates of the Registrant, based upon the last sale price of the Common Stock reported on the Nasdaq National Market on June 30, 2002, was $481,390,000. Shares of Common Stock held by each officer, director, and holder of 5% or more of the outstanding Common Stock have been excluded in that such persons may be deemed to be affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

On March 14, 2003 approximately 26,443,805 shares of the Registrant s Common Stock, $.001 par value, were outstanding.

Certain parts of the Registrant s Proxy Statement relating to the Annual Meeting of Stockholders to be held on May 15, 2003 (the Proxy Statement) are incorporated by reference into Part III of this Annual Report on Form 10-K.

SPECIAL NOTE ON FORWARD-LOOKING STATEMENTS

This Report on 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, which are subject to the safe harbor created by those sections. The forward-looking statements are based on the Registrant s current expectations and projections about future events. In some cases, forward-looking statements can be identified by terminology such as may, will, should, could, predicts, potential, continue, expects, anticipates, future, inter estimates, and similar expressions. In particular, we have included forward-looking statements regarding the following: (i) our anticipated financial results for 2003; (ii) the timeline and potential results of preclinical development and clinical trials; (iii) potential outcomes of our and Abbott s litigation with Novartis; (iv) our plans for marketing a cyclosporine capsule in Europe; (v) anticipated expenditures and timing relating to FDA and foreign approval of our products and facilities; and (vi) anticipated potential strategic collaborations with others. These forward-looking statements are made as of the date of this Report on Form 10-K. These forward-looking statements are based on current beliefs, expectations and assumptions and involve certain risks and uncertainties that could cause actual results, levels of activity, performance, achievements and events to differ materially from those implied by such forward-looking statements. The cautionary statements made in this Report on Form 10-K should be read as being applicable to all related forward-looking statements wherever they appear. Our actual results could differ materially from those discussed here. Factors that could cause or contribute to such differences include those discussed in Risk Factors, as well as those discussed elsewhere herein. The Registrant disclaims any obligation to update these forward-looking statements.

SANGSTAT MEDICAL CORPORATION

FORM 10-K
FOR THE FISCAL YEAR ENDED DECEMBER 31, 2002

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PART I

TRADEMARKS

SangStat®, Thymoglobulin®, Thymoglobuline®, Lymphoglobuline® and Celsior® are registered trademarks of SangStat Medical Corporation or its subsidiaries and Gengraf™ is a trademark of Abbott Laboratories, Inc.

PART I

ITEM 1. BUSINESS

Overview

SangStat is a global biopharmaceutical company focused on immunology and working to discover, develop and market high-value therapeutic products in immunology, transplantation medicine, hematology/oncology and auto-immune disorders. Since our incorporation in 1988, we have been dedicated to improving the outcome of organ and bone marrow transplantation through the development and marketing of products that address transplantation in the worldwide market. We are headquartered in Fremont, California. We maintain a strong European and U.S. presence, including direct sales and marketing forces in all major European markets, the U.S. and Canada and distributors throughout the rest of the world.

Our primary marketed product, Thymoglobulin, a treatment for acute rejection of a kidney transplant, was launched in the U.S. in February 1999. Thymoglobulin achieved worldwide sales of $37.9 million in 2000, $51.4 million in 2001 and $69.5 million in 2002. The success of Thymoglobulin and its potential in areas beyond solid organ transplantation have provided us with the ability to examine and develop new therapeutic opportunities outside of transplantation.

We are now focusing on a variety of therapeutic products and product candidates to address the pre-transplant, acute care and chronic phases of transplantation as well as product candidates in immunology, hematology/oncology and auto-immune disease.

We currently sell the following products:

- Thymoglobulin® (also sold under the name Thymoglobuline® outside the U.S.);
- Gengraf® cyclosporine capsule (co-promoted with Abbott Laboratories in the U.S.);
- Lymphoglobuline® (outside the U.S.); and
- Celsior®.

Our principal products in research and development include:

- A smaller-size cyclosporine capsule;
- RDP58; and
- Humanized polyclonal antibodies.

Background

Organ Transplantation

Organ transplantation can save or improve the lives of patients with organ failures. Transplantation involves surgically replacing the diseased or failed organ of a transplant recipient with a healthy organ from a donor.

In order to prevent rejection of implanted organs, most recipients must begin a life-long regimen of immunosuppressive therapy immediately upon receiving a donated organ. This immunosuppressive regimen usually requires daily therapy in order to prevent organ rejection and graft loss. Products that supplement immunosuppression can reduce the frequency and severity of rejection and infection episodes. These products can potentially enhance patient outcomes, while providing potential cost savings in the treatment of transplantation and its associated side effects. Our product Gengraf, an immunosuppressant, is approved in the U.S. for the prevention

of kidney, liver and heart rejection.

The Transplant Immune Response

The function of the immune system is to protect the body from damage caused by invading microorganisms or other foreign matter. Differences between a donor s and a recipient s antigens can lead to the recognition of the donor s organ as foreign matter by the recipient s immune system. Specifically, the donor organ antigens are recognized by the immune system of the graft recipient as being non-self, triggering the immune system to attack and invade the graft. When the recipient s immune system attacks and invades the donated graft, rejection and loss of the graft often occur. Thymoglobulin is approved for acute kidney graft rejection in the U.S., and Thymoglobulin and Lymphoglobuline are approved for both prevention and treatment of acute graft rejection in various countries outside the U.S.

The Transplant Process

A typical transplant patient progresses through three phases:

The Pre-Transplant Phase

A transplant candidate is registered on a national computerized waiting list. A candidate usually waits months or even years for a compatible organ. Organs harvested from donors are stored in a preservation solution such as our product Celsior to prevent organ deterioration. Each organ is cross-matched with potential recipients. The organ is then shipped in the same organ preservation solution to the recipient s transplant center.

The Acute Phase (Surgery and First Year Post-Transplant)

After transplantation, the physician must prevent graft rejection for the transplant to be a success. Consequently, the success of the transplant is highly dependent on the immunosuppressive regimen that is initiated at the time of transplantation and continued daily for the rest of the patient s life. Organ recipients must be regularly monitored to measure the body s immune response and blood drug levels and to help identify acute rejection episodes. Many patients undergo one or more rejection episodes in the first year after transplant and require additional immunosuppressants such as our Thymoglobulin product.

The Chronic Phase (Lifetime Post-Transplant)

The use of immunosuppressants such as cyclosporine (including the Gengraf cyclosporine capsules we distribute), initiated during the acute phase, is continued daily throughout the patient s lifetime to minimize or prevent the loss of the organ by rejection. These drugs impair the recipient s immune system in order to reduce the immune response against the graft. Even with the use of immunosuppressants, patients are always at risk of losing a transplanted organ through acute or chronic rejection.during the first three years following transplantation. Chronic use of immunosuppressants can also lead to serious side effects, including life-threatening infections, kidney or liver toxicity and cancer.

Aplastic Anemia

Aplastic anemia, which primarily affects young people, is a disease in which the stem cells disappear from the bone marrow. Aplastic anemia has a high mortality rate and, even with treatment, quality of life is poor. A lack of stem cells in the bone marrow inhibits the production of blood cells. As a result, patients with this disease are dependent on weekly blood transfusions that require frequent visits to the physician s offices. Both Thymoglobulin and Lymphoglobuline are approved in certain countries outside of the U.S. for treatment of aplastic anemia, and we believe that the majority of sales of Lymphoglobuline in Japan are for the treatment of aplastic anemia. Current treatments for severe aplastic anemia include immunosuppressants and, if necessary, bone marrow transplantation.

Bone Marrow or Stem Cell Transplantation

Bone marrow or stem cell transplantation is a standard therapy for many disease states, primarily cancer or pre-cancerous diseases. Stem cells, found in the peripheral blood or in the bone marrow, are given by an intravenous infusion to re-establish marrow function in a patient after ablation of the patient s bone marrow.

Immunosuppressive therapy, primarily anti-thymocyte globulin, or ATG, such as Lymphoglobuline and Thymoglobulin, chemotherapeutic agents and/or irradiation are given as part of a conditioning regimen. The goal of this regimen is threefold: to limit the patient s ability to mount an immune response to the new bone marrow or stem cells, to provide space for the new cells, and to destroy any residual cancer if the patient is being treated for a malignancy.

Some of these patients experience graft versus host disease, or GVHD. This is a condition in which the graft (i.e. the new immune system) begins to reject the host (i.e. the body). GVHD is a life-threatening complication that frequently occurs following an allogeneic bone marrow transplant. An allogeneic bone marrow transplant procedure involves transferring donor hemopoetic stem cells, the graft, from a healthy person into an immunosuppressed patient, the host. The transplant is intended to restore normal circulating blood and immune cells to a patient whose own hemopoetic and immune system has been ablated by the treatment of an underlying disease such as cancer and the conditioning regimen. Often a portion of the donor graft recognizes the host s own cells as foreign, becomes activated and attacks them, resulting in GVHD. GVHD typically involves damage to multiple organ systems, including the skin, liver and intestines. Thymoglobulin and Lymphoglobuline are approved for the treatment of steroid resistant GVHD in various countries outside the U.S.

Myelodysplastic Syndrome (MDS)

Myelodysplastic Syndrome, or MDS, also referred to as pre-leukemia, is a rare disease in which the bone marrow functions abnormally and does not produce enough normal blood cells. Weekly blood transfusions remain the principal therapy for less advanced types of MDS. Current treatments for the advanced types of the disease include chemotherapy and/or bone marrow transplantation.

Crohn s Disease and Ulcerative Colitis

Crohn s disease and ulcerative colitis are similar diseases that are often grouped together as inflammatory bowel disease. Industry sources estimate that there may be up to 1,000,000 Americans who suffer from inflammatory bowel disease. Crohn s disease is a chronic inflammatory disease of the gastrointestinal tract that usually causes diarrhea, abdominal pain, fever and rectal bleeding. Ulcerative colitis is a similar disease to Crohn s disease, but only infects the large intestine and is characterized by inflammation and ulceration of the innermost lining of the colon. Symptoms include diarrhea and sometimes abdominal pain. We are developing RDP58 for the treatment of both Crohn s disease and ulcerative colitis.

Chemotherapy-Induced Diarrhea

Chemotherapy-induced diarrhea is a significant gastro-intestinal complication from treatment of cancer with certain chemotherapeutic agents. CPT-11 is the most active drug against colon adenaocarcinoma, a form of colon cancer. Diarrhea is the most common side effect that limits the amount of CPT-11 that patients can tolerate. Prevention of diarrhea may increase patients tolerance of the dose of CPT-11, potentially increasing

their response to this treatment.

Products and Product Candidates

The following table summarizes our principal products and product candidates.

Marketed Product	Indications/Potential Clinical Use	Status	Marketing Rights
Thymoglobulin/ Thymoglobuline	Prevention and treatment of acute graft rejection in solid organ transplantation, treatment of severe aplastic anemia and steroid resistant GVHD	U.S.: Approved for treatment of acute kidney rejection episodes EU: Approved for prophylaxis and treatment of rejection in kidney, heart, pancreas, and liver transplants; treatment of acute GVHD in allogeneic bone marrow transplantation; and treatment of aplastic anemia	SangStat
Gengraf	Chronic immuosuppression (prevents organ rejection)	U.S.: Approved	SangStat and Abbott Laboratories jointly (U.S.)
Lymphoglobuline	Prevention and treatment of acute graft rejection in solid organ transplantation, treatment of severe aplastic anemia and steroid resistant GVHD	Over 50 countries other than the U.S.: Approved	SangStat
Celsior	Preservation of organs prior to transplantation	U.S.: Approved for cardiac transplantation EU: Approved for cardiac and abdominal organ transplantation	SangStat

Product Candidate	Indications/Potential Clinical Use	Status	Commercialization Rights
Smaller-Size Cyclosporine Capsule	Chronic immunosuppression (prevents organ rejection)	Marketing authorization applied for in a European country	SangStat
RDP58	Ulcerative colitis, Crohn s disease	Phase IIa	SangStat
RDP58	Chemotherapy Induced Diarrhea	Phase Ib	SangStat

Future Technology	Indications/Potential Clinical Use	Status	Commercialization Rights
Humanized Polyclonal Antibodies	Hematological cancers; autoimmune disease	Research	SangStat and Therapeutic Human Polyclonals, Inc.

Marketed Products

Thymoglobulin

Thymoglobulin is a pasteurized anti-thymocyte rabbit immunoglobulin that induces immunosuppression as a result of T-cell depletion and immune modulation. Thymoglobulin is made up of a variety of antibodies that recognize key receptors on T-cells, the cells of a transplant recipient s immune system that recognize and ultimately reject foreign objects such as transplanted organs. While the exact mechanism is unknown, researchers believe Thymoglobulin antibodies may inactivate and kill these T-cells, thus neutralizing the rejection process and allowing the transplanted organ to recover. Thymoglobulin is also used to treat aplastic anemia and steroid resistant GVHD. Thymoglobulin is approved in the U.S. only for treatment of kidney transplant acute rejection episodes.

Market

We market Thymoglobulin in over 50 countries directly or through our distributor, with a majority of our revenues coming from Europe and the U.S. We launched Thymoglobulin in the U.S. in February 1999. Thymoglobulin is currently approved for treatment of acute rejection in kidney transplant recipients in the U.S. In other countries where Thymoglobulin is marketed, it generally has the following indications:

prophylaxis and treatment of rejection in kidney, heart, pancreas, and liver transplants;
treatment of acute steroid resistant GVHD in allogeneic bone marrow transplantation; and
treatment of aplastic anemia.

We market and sell Thymoglobulin in Western Europe and North America. Outside those territories, we market through Aventis or through other distributors.

Additional Clinical Studies

Induction/Prevention

We have completed a comparative induction study of Thymoglobulin versus Simulect, a monoclonal antibody marketed by Novartis Pharmaceuticals Inc. for certain high-risk renal transplants. Our intent in this study was to generate data comparing the clinical effects of Thymoglobulin with Simulect. It was not our intent to use this trial, and the FDA has indicated that this trial will not be sufficient, to support label indication changes or expansion. This prospective, randomized, open-label study was conducted in over 20 transplant centers in the U.S. and Europe. Primary endpoints at 6 months were graft survival, patient survival and incidence of acute rejection. We also captured other important clinical data such as infections and incidence of delayed graft function. The study was closed early in March 2002, with a total enrollment of 279 participants out of a planned 340,after an interim analysis revealed significantly fewer acute rejections of implanted kidneys in patients treated with Thymoglobulin versus Simulect. In the interim analysis, the incidence of acute kidney rejection was 2.5 times greater among patients treated with Simulect compared to patients who received Thymoglobulin and this was statistically significant. Further, there was no statistically significant difference in the rate of severe adverse events in either arm of the study. These interim results are preliminary and subject to change upon finalization of the study results.

Gengraf® Cyclosporine Capsules

Cyclosporine, first approved in the U.S. in 1983, is a potent immunosuppressive agent. Cyclosporine inhibits the synthesis and release of the cytokine interleukin-2, which is essential to the body s immune response to transplanted organs. The Gengraf cyclosporine capsule, a product of Abbott Laboratories, Inc., is a generic version of Neoral® capsules, which is marketed by Novartis. SangStat and Abbott co-promote and distribute Gengraf in the U.S. Gengraf is a chronic therapeutic normally taken daily over the lifetime of the organ recipient to prevent organ rejection.

Cyclosporine Market

Cyclosporine is a leading immunosuppressive drug used to prevent organ and graft rejection in transplantation. The majority of these patients are prescribed daily doses of cyclosporine for the rest of their lives. Cyclosporine is also indicated for the treatment of rheumatoid arthritis and adult non-immunocompromised psoriasis patients. Worldwide sales of cyclosporine are approximately $1 billion per year.

We entered into an agreement with Abbott in May 1999 for the co-promotion, distribution and research in the U.S. of Gengraf and SangCya Oral Solution. SangCya Oral Solution, which is a generic version of Neoral oral solution, was withdrawn from the U.S. market in July 2000 and is currently not sold.

We launched Gengraf cyclosporine capsules in May 2000 in the U.S. through our combined SangStat/Abbott sales force. Gengraf s indications are identical to Neoral s indications and include (i) the prophylaxis of organ rejection in kidney, liver and heart allogeneic transplants; (ii) the treatment of patients with severe, active rheumatoid arthritis where the disease has not adequately responded to methotrexate; and (iii) the treatment of adult, non-immunocompromised patients with severe (i.e. extensive and/or disabling), recalcitrant, plaque psoriasis who have failed to respond to at least one systemic therapy (e.g. PUVA, retinoids or methotrexate), or in patients for whom either systemic therapies are contraindicated or cannot be tolerated. Our ability to continue marketing Gengraf may be limited as a result of a recent judgment that Gengraf infringed a Novartis patent.

Lymphoglobuline®

Lymphoglobuline is an anti-thymocyte equine immunoglobulin that induces immunosuppression as a result of T-cell depletion and immune modulation. In certain countries outside the U.S., it is approved for the prevention and treatment of rejection episodes in kidney, heart, pancreas, or liver transplantation. In hematology, Lymphoglobuline is approved in certain countries outside the U.S. for treatment of aplastic anemia and in the treatment of steroid resistant GVHD.

Market

We (or our distributors) market Lymphoglobuline in over 50 countries outside the U.S. Our sales force markets this product in Western Europe and Canada. Outside these countries, we sell Lymphoglobuline through our distribution agreement with Aventis or through other distributors. Aventis markets this product in Japan, where we believe a high percentage of sales occur for treatment of aplastic anemia. We hope to address U.S. market opportunities for Lymphoglobuline with the sale of Thymoglobulin. Therefore, we have no plans to seek approval for Lymphoglobuline in the U.S.

Celsior®

Celsior is a storage solution for organs after removal from the donor and before transplantation into the recipient. It is a sterile, nonpyrogenic, extracellular solution for hypothermic flushing and storage of hearts. Early graft loss remains a significant problem associated with cardiac transplantation and damage to the heart tissue can occur due to inadequate preservation. Effective organ preservation includes initial flushing of the heart tissue during the recovery process and cold storage while the donor heart is transported to the recipient. Celsior is the first and only flush and cold storage solution approved by the FDA, as a medical device for cardiac transplantation. It was designed specifically for cardiac transplantation to minimize myocardial edema, oxygen free radical-induced reperfusion injury, and diastolic stiffness.

Market

We market Celsior throughout Europe, and we commenced marketing the product in the U.S. in September 1999. Celsior is approved for marketing in the U.S. only in connection with cardiac transplantation. We are selling Celsior in Europe also for abdominal organ (kidney, pancreas and liver) flushing and storage. Outside of Western Europe and North America, we sell Celsior through our distribution agreement with Aventis or through other distributors.

Principal Products in Development

Consistent with our strategic changes in October of 2000, we leveraged our success with Thymoglobulin to expand our research and development initiatives to include areas outside of transplantation, including immunology,

hematology/oncology and auto-immune disease. Our research and development expenses were $20.8 million in 2000, $17.9 million in 2001 and $18.9 million in 2002. These expenses primarily relate to additional indications for marketed products and new products in development.

We currently have two principal products in development:

Cyclosporine Capsules

We have an exclusive license to a pending patent application on a novel smaller-size cyclosporine capsule formulation from Tris Pharma, a small U.S. research and development company. We expect that the capsule will be smaller than currently marketed cyclosporine capsules. We filed regulatory application for marketing approval in a European country in January 2003. We intend to follow the European Community Mutual Recognition Procedure for obtaining marketing authorization in multiple member states following initial approval.

RDP58

RDP58 is a novel inhibitor of several inflammatory cytokines, notablyTNF-alpha. Interleukin(IL) 2, IL12, and Interferon (IFN)-gamma are also inhibited. RDP58 is currently in Phase IIa clinical trials in Europe. This is our first product candidate from our own research and development efforts to enter such a clinical trial. RDP58 was designed using our drug design approach, in collaboration with Synt:em, that integrates advanced biology, biophysics, chemistry and information technology in a coordinated effort to design and develop potential therapeutic products. We are investigating the use of RDP58 for treatment of various auto-immune disorders. Ulcerative colitis and Crohn s disease are the two auto-immune disorders being examined in the current Phase II study.

Overview

Cytokines are protein messengers that coordinate the functions of immune cells and certain other cells and tissues. TNF-alpha is a cytokine that, when released in excess, can trigger activation of immune responses and inflammation. Continuous excessive TNF-alpha release can cascade into a variety of auto-immune diseases including inflammatory bowel disease, rheumatoid arthritis and psoriasis. There are currently a number of therapeutic products that target inhibition of TNF-alpha release. TNF inhibitors, including Remicade and Enbrel, have been approved for treatment since 1998 and 1999, respectively. They are considered the standard of care in the treatment of a variety of auto-immune diseases including Crohn s disease and rheumatoid arthritis. These therapeutic agents are being examined as a treatment for a number of other auto-immune diseases, including psoriasis, psoriatic arthritis and ankylosing spondylitis. RDP58 inhibits production of other cytokines that contribute to the inflammatory process. In addition to TNF-alpha, we have determined that RDP58 inhibits IFN-gamma, IL12 and IL2. RDP58 decreases IFN-gamma production by regulating IFN-gamma gene expression. Studies are in progress to understand how IL2 and IL12 are inhibited.

Animal models, including studies in primates, suggest that RDP58 could decrease levels of TNF-alpha, reduce inflammation, and improve clinical outcomes. Currently marketed TNF-alpha inhibitors work by binding to TNF-alpha after synthesis and excretion by the cell, thus neutralizing TNF-alpha in the blood before it can participate in the inflammatory response. In contrast, we believe RDP58 prevents the translation of TNF-alpha RNA, thereby preventing the synthesis of TNF-alpha protein within the cell. We believe that RDP58 could be a more efficient inhibitor of TNF-alpha as it prevents the synthesis of the protein as opposed to current therapy, which attempts to inhibit the effects of its expression post-synthesis.

RDP58 is currently being tested in an oral formulation consisting of D-isomer amino acids. This peptide is resistant to enzymatic breakdown during the digestive process, which is important for any oral therapeutic agent. Current TNF-alpha inhibitors are only available in non-oral form, either through a subcutaneous injection or through intravenous administration.

Clinical Studies

Inflammatory Bowel Disease. We filed for Clinical Trial Exemption (CTX) with the U.K. Medicines Control Agency (the U.K. equivalent to the U.S. FDA) for RDP58 in September 2001 after successful completion of a Phase I normal volunteer dose escalation safety study. In the Phase I study, three groups of nine healthy volunteers participated in a dose escalation study using 3 doses for a total of 28 days. Oral RDP58 was found to be safe and

well tolerated. The CTX allowed us to initiate Phase II proof-of-principle, dose-ranging clinical trials in the fourth quarter of 2001. The Phase II trials are prospective, randomized, blinded trials in patients with mild-to-moderate ulcerative colitis or Crohn s disease. We completed patient enrollment and expect to announce the results of these studies in the second quarter of 2003. As our lead and primary product in development, adverse or inconclusive results from this trial would have a significant and material adverse effect on our research and development program and our prospects.

Chemotherapy Induced Diarrhea. RDP58 has been shown to significantly decrease the incidence of diarrhea and mortality in a murine model of CPT-11 toxicity. In this model, 93% of mice given 200mg/kg of CPT-11 developed diarrhea and had a 63% mortality rate. In the study, of the mice that were given RDP58 in their drinking water starting three days before treatment with CPT-11, only 33% developed diarrhea and 93% of the animals survived. Our preclinical studies show that when RDP58 is given concurrently, the maximum tolerated dose of CPT-11 is increased.

In addition, TNF-alpha, IFN-gamma, and IL12 production in the gut are at normal levels. When tested in an animal model of cancer, RDP58 allowed the CPT-11 dose to be doubled resulting in a greater than 80% reduction in tumor volume compared to about 40% reduction at the lower concentration. RDP58 by itself did not affect the rate of tumor growth.

We have filed an Investigative New Drug (IND) with U.S. FDA under which we have begun a U.S. Phase Ib safety study of RDP58 for chemotherapy induced diarrhea (CID). The purpose of the study is to investigate the safety of RDP58 in patients who are undergoing chemotherapy treatment. We have begun enrollment and expect to complete the study by the end of 2003 or early 2004.

Other Preclinical Developments

RDP58 is the subject of five additional development programs: interstitial cystitis, neurology, HIV, dermatology and pulmonary.

Interstitial Cystitis. Interstitial cystitis, or IC, is a chronic inflammation of the bladder resulting in frequent and urgent urination that is accompanied with lower abdominal or urethral pain. Recent epidemiological data suggest that there may be greater than 700,000 cases of IC in the US. Three general treatment approaches are: oral medication, intravesical therapy (bladder instillation) or surgery. Surgery is indicated for those patients that have failed the other two approaches, and multiple forms are used. The only FDA approved oral drug specifically for IC is pentosan polysulfate sodium, a derivative of heparin sulfate, which is presumed to treat the lining of the bladder to restore normal function. Other oral medications include analgesics (pain relievers), anti-depressants, antihistamines and muscle relaxants. The more common intravesical therapies consist primarily of intravesical (inserted by a catheter through the urethra) instillation of DMSO, heparin sulfate, Bacillus Calmette-Guerin, or a cocktail of drugs. According to the Interstitial Cystitis Association, at this time there is no cure for IC, nor is there an effective treatment which works for everyone. Preliminary studies in a mouse model of IC showed that RDP58 may have therapeutic activity in IC. Mouse bladders were inflamed by intravesical instillation of lipopolysaccharide (LPS), a potent inflammatory compound. Histological analysis (viewing tissues under a microscope) showed heavy infiltration of leukocytes (immune cells) and severe edema (swelling). Treatment with RDP58 after LPS instillation reduced these indicators of inflammation on average by 70%.

Neurology. RDP58 was studied in a standard experimental model simulating the symptoms of multiple sclerosis or MS, in rats. Animals were immunized with myelin basic protein to develop an autoimmune response resulting in paralysis of the tail and hind limbs. When RDP58 was given as a single dose via intra-cerebroventricular (in a cavity of the brain) injection, it dramatically diminished the onset of paralysis. In some animals, paralysis was completely prevented. The beneficial effects were best when RDP58 was given up to 10 days after inoculation with myelin basic protein when clinical symptoms were beginning to appear.

The currently approved standard of care for the treatment of MS is beta-interferon. Beta-interferon as a treatment regimen is most efficacious when commenced at the earliest point in the disease s progression, usually immediately after diagnosis and before any symptoms of the disease present themselves. Furthermore, beta interferon has been shown to be increasingly ineffective as the disease progresses and has shown little efficacy in minimizing or halting symptoms, such as paralysis, after they present themselves in a patient. We believe that RDP58 presents a unique opportunity in multiple sclerosis as our preclinical models demonstrate that disease progression may be halted after the presentation of symptoms.

HIV Gastro-intestinal disorders. Diarrhea related to HIV is a significant gastro-intestinal disorder affecting HIV-infected persons. HIV-related diarrhea is a malabsorption syndrome that results in nutrient loss and poor drug absorption. This translates into increased weight loss and viral titers in patients who suffer from HIV-related colitis. Researchers at the University of California at Davis, with the support of scientists at SangStat, were awarded a National Institute of Health grant to study the impact of RDP58 on the gastro-intestinal complications of HIV in the HIV primate model. In this study, RDP58, when given with anti-viral therapy, was found to enhance the rate of repopulation of the CD4+ and CD4+CD8+ lymphocyte populations in the gastrointestinal mucosa compared to animals receiving anti-viral therapy only.We expect to explore this finding in a pilot clinical trial.

Dermatology. TNF-alpha appears to play an important role in psoriasis and possibly in atopic dermatitis. RDP58 has been fashioned into a topical gel that will be used to determine efficacy in these two dermatologic diseases. Animal toxicology studies are underway. Preliminary results in a mouse model of skin inflammation showed that, RDP58, when applied to the affected skin, reduces TNF-alpha expression, edema (swelling), and inflammatory cell infiltration.

Pulmonary. RDP58 is a powder formulation that may be used as an aerosol to provide inhalation therapy for asthma, chronic obstructive pulmonary disease, sarcoidosis and other pulmonary diseases. Preliminary data in animal models of Pulmonary Fibrosis (PF) and Chronic Obstructive Pulmonary Disease (COPD) show that RDP58 significantly reduces TNF-alpha levels and inflammatory cell infiltration in the lungs. We are pursuing partners to continue development in this therapeutic arena.

Sales and Marketing

In the U.S., we market products through our direct sales force. As of December 31, 2002, we had 21 account managers, supervised by 3 regional sales directors, who call on or sell primarily to the approximately 260 transplant centers in the U.S. A number of the account managers have backgrounds in transplantation, either from selling other transplant products or with clinical backgrounds as nurses or as transplant coordinators in transplant centers. We also have two national account directors who call on group purchasing organizations and managed care groups.

Sales to Cardinal Health Inc., McKesson Corporation, AmeriSource and Bergen Brunswig Drug Company accounted for 28%, 19%, 14% and 15%, respectively, of total revenues in 2002, and 26%, 18%, 12% and 11%, respectively, of total revenues in 2001. Sales to Cardinal Health Inc. and McKesson Corporation accounted for 13% and 15%, respectively, of total revenues in 2000.

As of December 31, 2002, we had approximately 39 sales and marketing people throughout the major European markets.

Strategic Relationships

We evaluate on an ongoing basis potential collaborative relationships with corporate and other partners where such relationships may complement and expand SangStat s research, development, sales and marketing capabilities.

Therapeutic Human Polyclonals

In November 2002, we entered into a collaboration with Human Therapeutic Polyclonals, Inc. or THP for the development of humanized polyclonal therapeutic products to be generated by the immune systems of transgenic animals. THP is a private research stage company that was formed by two scientists, one of whom, Dr. Roland Buelow, was our Senior Vice President of Discovery Research from April 1, 2000 to November 8, 2002. Dr. Buelow is transitioning from his employment with us to become the full-time Chief Scientific Officer of THP.

THP was formed to develop animals whose immune systems have been genetically altered so that they would produce antibodies that contain human, instead of animal, sequences. The engineered animals would then be injected with proteins called antigens that are found primarily on disease-producing cells, viruses or other pathogenic (disease-causing) materials. For example, antigens that mark certain cancer cells could be injected. The animal s altered immune system would then produce antibodies that react against the antigen and, hence, against the disease target (for example, the cancer cell). These antibodies would be extracted from the animal s blood and purified for human use. THP s first genetic engineering effort is focused on rabbits, which produce high quantities

(titers) of antibodies. Our primary marketed product, Thymoglobulin, is a rabbit antibody product made in a similar fashion from non-engineered rabbits. Consequently, our expertise in producing pharmaceutical-grade polyclonal antibodies from rabbits fits well with THP s plans to develop antibodies from transgenic rabbits. Animal antibodies generally have limited utility, since they normally produce an immune reaction against them when injected into humans. By humanizing the antibodies, THP hopes to reduce or eliminate these reactions.

Current humanized antibody products such as Rituxan® and Herceptin® are monoclonal antibodies. The antibodies in these products are all identical and identify only a single point (epitope) on the antigen. By contrast, the antibodies produced directly by live animals have significant variability and react against many epitopes of the antigen. These antibodies are called polyclonal antibodies. Because they react to many epitopes, polyclonal antibodies have the potential to be more effective than monoclonal antibodies, since disease targets may contain different epitopes.

Another potential advantage of the THP system is that commercial quantities of the antibodies are produced directly from colonies of rabbits, which we anticipate will be very similar to production of our Thymoglobulin product. By contrast, current humanized monoclonal antibody products must first be developed from a mouse or synthetic system, and then cloned into a production cell line. The commercial quantities of humanized monoclonal antibody products are made in complex and expensive bioreactor factories where the cells lines are cultivated.

Antibodies have two different components: the constant region that is the same for each antibody, and the variable region that varies and codes for a specific antigen. Currently, THP has produced rabbits that produce antibodies with part of the constant region that is human. THP s first objective is to develop a proof-of-principle rabbit that produces antibodies with fully human constant regions within a year. Because the research is at an early stage, clinical products from the technology are not expected to reach the market for years, if ever.

We have options from THP to obtain exclusive licenses to the THP technology to produce humanized polyclonal antibody products. One option is for a humanized version of our current Thymoglobulin product. We also have options to obtain exclusive licenses to products to treat hematology (blood related) diseases, such as leukemia and lymphoma. The options have an exercise period that commences when THP has produced a genetically engineered rabbit capable of producing commercial-grade humanized antibodies. Each license would have an up-front

fee, milestone payments based on progression through clinical trials to product approval, and royalties. THP has the right to contribute to the development costs for hematology products and receive a commensurate share of profits from commercial sales. We share antibody purification know-how with THP. In November 2002, we made a one-time technology access fee payment to THP of $500,000 under the terms of the agreement.

Additionally, we have made an equity investment of $3.2 million in THP and are committed to make a second investment of $3.2 million when THP has produced the proof-of-principle engineered rabbit, unless that milestone is unduly delayed. The total of these investments would represent ownership of approximately twenty percent (20%) of the issued share capital of THP. Our investments are made in conjunction with investments by Research Corporation Technologies, Inc., which provided start-up financing for THP and is the majority shareholder of THP. When THP has produced the commercial-grade engineered rabbit, we have an option to make an additional equity investment of $15.0 million, which would give us ownership of approximately 40% of THP s issued share capital. We do not have the right to acquire full ownership of THP.

Abbott Laboratories

In May 1999, we signed a multi-year co-promotion, distribution and research agreement with Abbott for Gengraf in the U.S. We are the exclusive distributor for Gengraf and share marketing, promotional and development expenses as well as the profits from the co-promotion of the product with Abbott. The agreement for Gengraf involves only sales in the U.S. The agreement ends December 31, 2004 unless both companies agree to extend it. Pursuant to this agreement, Abbott made an equity investment of $14 million during 1999 in exchange for approximately 894,000 shares of common stock, representing a premium to fair market value at that time aggregating to $1.3 million. In addition, Abbott made a series of up-front and milestone payments totaling $20.8 million, including $6.9 million received in 2000, and a long-term loan of $16.0 million to us received during 1999. In January 2000, we made a milestone payment of $4.0 million to Abbott under the terms of the agreement. No further milestone payments are required from either company. All up-front and milestone payments received, net of milestone payments made, and the premium received on the sale of common stock to Abbott are recorded as deferred revenue and recognized ratably over the term of the agreement as revenue from collaborative agreements. In May 2000, Abbott and we

launched Gengraf, the cyclosporine capsule developed by Abbott. In connection with the equity investment, Abbott and we entered into a Right of First Refusal Agreement and a Registration Rights Agreement, and amended and restated our existing Supply Agreement. We have repaid $11.0 million of the loan and $5.0 million remains outstanding. Our ability to continue marketing Gengraf may be limited as a result of a recent judgment that Gengraf infringed a Novartis patent.

Abgenix

In August 2000, we entered into a global co-development, supply and license agreement with Abgenix, Inc., for ABX-CBL, an antibody developed by Abgenix. We made an initial license fee payment of $1.0 million to Abgenix. ABX-CBL is an anti-CD147 monoclonal antibody for the treatment of steroid resistant GVHD and is currently in a multicenter, randomized, and controlled Phase II/III study. Development costs are shared equally. We also have the right, subject to the terms and conditions of the agreement, to commercialize other anti-CD147 antibodies developed by Abgenix.

In February 2003, preliminary results of the Phase II/III study showed no survival advantage with ABX-CBL compared to the control arm of the study. Consequently, we and Abgenix decided to discontinue further development of ABX-CBL. As a result, we will not have to pay Abgenix two additional payments of $1.0 million that were contingent on achievement of certain milestones. We also do not have to reimburse Abgenix for development expenses incurred prior to January 1, 2000 since that reimbursement was payable only after product launch. The amount had not been determined, but the agreement limited our obligation to $6,100,000. We were required to reimburse Abgenix for one-half of the development costs incurred for ABX-CBL from January 1, 2000 to August 8, 2000, with our share being approximately $1.9 million. We paid Abgenix $1.4 million as of December 31, 2001 and the remaining $0.5 million was paid in 2002. The license fee and the reimbursement of development expenses are recorded as research and development expenses.

Aventis

We entered into a Distribution Agreement with Aventis in May 1999 that appointed Aventis as our exclusive distributor outside North America and Western Europe. The agreement automatically extends for additional annual periods unless either party gives notice of termination, and the current expiration date is March 31, 2004. Aventis sells our products either through its local subsidiaries or through third party distributors that often distribute other Aventis products. We are in the process of renegotiating the Aventis contract to remove territories from the contract. We then would contract directly with a local distributor in that territory, which may be the local Aventis subsidiary in that territory. We have contracted directly with local distributors in Israel and certain countries in Eastern Europe, South and Central America, and Asia.

Aventis also performs some of the steps in the manufacturing process of Thymoglobulin and Lymphoglobuline. In addition, we pay Aventis royalties on Thymoglobulin and Lymphoglobuline contingent upon the sales of these products. In 2000, 2001 and 2002, royalty payments on Lymphoglobuline and Thymoglobulin to Aventis totaled approximately $622,000, $2.2 million and $7.6 million, respectively. We expect these royalty payments to increase in future years since we began paying royalties on Thymoglobulin during the third quarter of 2001. The royalty payments on Thymoglobulin increased on the third anniversary of the purchase of IMTIX (October 1, 2001) and will decrease again three years thereafter.

Synt:em

In July 2001, we entered into a three-year research collaboration agreement for the discovery of next generation RDP58 molecules with Synt:em, a French biopharmaceutical company. The aim of this collaboration is to design novel RDP58-like compounds for the inhibition of inflammation in new in vivo applications using Synt:em s proprietary rational design technology, Acti:map. The SangStat-Synt:em agreement builds on earlier development efforts between SangStat and Synt:em with Allotrap peptides that led to the original discovery of RDP58. Under the terms of the agreement, SangStat performs *in vitro* and *in vivo* testing of peptides and novel rationally designed peptides while Synt:em uses its Acti:map technology to perform the rational design work.

In late 2001, the European Community, or EC issued a research contract to a consortium consisting of our wholly owned French subsidiary, Imtix-SangStat SAS, and seven academic research centers. The grant covered a term of

three years and would provide up to approximately $2,755,600 (2,628,567 Euros) to the consortium to fund research in the role of heme oxygenase-1, or HO-1, in inflammation. Since RDP58 regulates HO-1, the research was of interest to Imtix-SangStat. A consortium agreement is being negotiated under which it is anticipated that the academic members of the consortium would convey to Imtix-SangStat the rights to commercialize any inventions arising in the course of the research. Under the EC research contract, Imtix-SangStat committed to funding approximately $471,500 (450,000 Euros) of research, with the EC matching that amount. Imtix-SangStat intended that a portion of its research would be subcontracted to Synt:em. Since the research of Synt:em currently being conducted under the SangStat-Synt:em Agreement is included under the EC contract, we are working with Imtix-SangStat and Synt:em to assign the SangStat-Synt:em Agreement to Imtix-SangStat.

Competition

The drug industry is very competitive. The drugs we market compete with existing and new drugs being created by pharmaceutical, biopharmaceutical, and biotechnology companies and universities. Many of these entities have significantly greater research and development capabilities, as well as substantial marketing, manufacturing, financial and managerial resources and represent significant competition for us. Many of the competitors have developed or are in the process of developing technologies that are, or in the future may be, the basis for competitive products. Some of these products may have an entirely different approach or means of accomplishing the desired therapeutic effect than products we are developing or marketing and may be more effective and less costly. In addition, many of our competitors have significantly greater experience than we do in conducting clinical trials of pharmaceutical products and obtaining regulatory approvals of such products. This could cause our competitors to succeed in commercializing products more rapidly than we can. The principal factors upon which our products compete are:

- product utility;
- therapeutic benefits;
- ease of use;
- pricing; and
- effective marketing.

We believe we generally compete favorably with respect to these factors. However, Thymoglobulin is the price leader in the U.S. and thus is exposed to competition from lower-priced products as pressures increase on health providers to contain costs.

Thymoglobulin and Lymphoglobuline compete with various products in the U.S. and worldwide. In the U.S., Thymoglobulin has been successful in establishing a market share against these products, most of which were all previously on the market. In the U.S. there is no competitor selling a rabbit antibody product similar to Thymoglobulin while in Europe there are a number of rabbit antibody competitors. Thymoglobulin has recently experienced increased competition from the off-label use of a newly introduced product. Increased competition from this or other products could affect the future sales or price of Thymoglobulin, which could have a material adverse effect on our business

and operating results.

Gengraf and our cyclosporine capsule in development are generic and compete against the branded cyclosporine product (Neoral®, produced by Novartis AG) as well as other generic cyclosporine products that have been or may be approved. These products also compete against Prograf®, marketed by Fujisawa Pharmaceutical Co. Ltd, and Rapamune®, marketed by Wyeth, which were approved by the FDA to be taken instead of cyclosporine.

RDP58 is an inhibitor of TNF-alpha synthesis. TNF-alpha is a cytokine released in excess in various autoimmune disorders. For that reason, many companies are pursuing development of a TNF-alpha inhibitor and we believe there could be substantial competition in this area. For example, Immunex/AHP s Enbrel® and Johnson & Johnson s Remicade® are both TNF-alpha inhibitors that are currently approved for rheumatoid arthritis and Crohn s disease, respectively.

Patents and Proprietary Technology

We have several issued patents in the U.S. that pertain to previous products and technologies that we do not intend to commercialize. Of our products, only Celsior is covered by issued patents. We have several pending patent applications on RDP58 and intend to vigorously pursue patent coverage for RDP58 and related products. We have no issued patents covering Thymoglobulin and Lymphoglobuline, and rely on our manufacturing know-how to protect these products. With respect to our cyclosporine capsules, we have in-licensed a pending formulation patent application from Tris Pharma.

In addition, as discussed above, we have also licensed certain patents and patent technology from others. We have an exclusive, worldwide license from Stanford University for certain issued patents and pending patent applications in the HLA and peptide area.

Patent applications in the U.S. are maintained in secrecy until patents are issued. Since publication of discoveries in the scientific or patent literature tends to lag behind actual discoveries by several months, we cannot be certain that we were the first to discover compositions covered by our pending patent applications or the first to file patent applications on such compositions. Our pending patent applications may not result in issued patents, our issued patents may not afford protection against a competitor and our products may infringe on other patents. Our ability to continue marketing Gengraf may be limited as a result of a recent judgment that Gengraf infringed a Novartis patent.

We also rely on trade secrets and proprietary know-how that we seek to protect, in part, by confidentiality agreements with our employees and consultants.

We have registered or applied for registration of the names of all of our marketed products and plan to register the names of our products under development once a name has been selected for the product candidate.

Manufacturing

Manufacturing pharmaceutical products is a highly regulated process. The FDA and other regulatory agencies require that manufacturing be done in accordance with current Good Manufacturing Practices, or GMP. Additionally, products can only be manufactured in facilities approved by the applicable regulatory authorities.

We acquired the unit near Lyon, France that manufactures Thymoglobulin and Lymphoglobuline in 1998. The FDA, as well as the Canadian and French health authorities, inspected this facility in February and March 2002 to ensure compliance with current regulatory standards. Currently Aventis performs some of the steps in the manufacturing process of Thymoglobulin and Lymphoglobuline under contract to us. We perform the remaining manufacturing steps ourselves in manufacturing facilities that we lease from Aventis. The agreements with Aventis expire on dates ranging from 2008 to 2013.

We have no other manufacturing facility and the Lyon facility could not be used for products other than biologics. Therefore, we rely on third parties to manufacture our other products, both those that we sell and those in development. We depend on such third parties to perform their obligations in compliance with all regulatory requirements and on a timely basis. If any of our contract manufacturers fail to perform, such failure may delay our clinical development or submission of products for regulatory approval or result in product shortages with respect to our marketed products.

With respect to raw materials, we have agreements for commercial scale production of cyclosporine bulk material with Gensia Sicor and Abbott Laboratories. Our Gensia Sicor agreement runs until December 31, 2005 and has an automatic one-year term renewal unless either party gives

notice. Our Abbott agreement terminates December 31, 2004 and is automatically renewed unless either party gives notice. Bulk cyclosporine is difficult to manufacture since it must be extracted from whole cells and carefully purified. We have sufficient quantities of bulk cyclosporine to meet our current needs. We believe we also have sufficient quantities of raw materials for our other products and product candidates.

Warehousing and Distribution

We use a logistics provider to store and distribute our products in the U.S. from one central warehousing location in

Memphis, Tennessee. When our provider receives a purchase order through electronic data input, phone, mail or facsimile, it sends the order to the warehouse for shipment, usually within 24 hours, to the customer placing the order. The provider is also responsible for invoicing and collections.

Government Regulation

Our research and development activities, preclinical studies and clinical trials, and ultimately the manufacturing, marketing and labeling of our products, are subject to extensive regulation by the FDA and other regulatory authorities in the U.S. and other countries (Regulatory Agencies). The U.S. Federal Food, Drug, and Cosmetic Act and the regulations promulgated thereunder and other federal and state statutes and regulations govern, among other things, the testing, manufacture, safety, efficacy, labeling, storage, record keeping, approval, advertising, promotion, import and export of our products and product candidates. Preclinical study and clinical trial requirements and the regulatory approval process typically take years and require the expenditure of substantial resources. Additional government regulation may be established that could prevent or delay regulatory approval of our product candidates. Delays or rejections in obtaining regulatory approvals would harm our ability to commercialize any product candidates we develop and our ability to receive product revenues. If regulatory approval of a product candidate is granted, the approval may include significant limitations on the indicated uses for which the product may be marketed.

Our products in clinical trials during the remainder of 2003 may include Thymoglobulin for expanded labeling and RDP58.

Our clinical trials may not be completed successfully or within any specified time period. Either the FDA or we may suspend clinical trials at any time, if either of us concludes that clinical subjects are being exposed to an unacceptable health risk, or for other reasons. The conduct of clinical trials is complex and difficult, especially in Phase III. Also the design or the performance of the Phase III clinical trial protocols may not be successful.

The results of preclinical studies and clinical trials, if successful, are submitted in an application to seek FDA approval to market the drug or biological product for a specified use. The testing and approval process requires substantial time and effort, and there can be no assurance that any approval will be granted for any product or that approval will be granted according to any schedule. The FDA may refuse to approve an application if it believes that applicable regulatory criteria are not satisfied. The FDA may also require additional testing for safety and efficacy of the drug. Moreover, if regulatory approval of a drug product is granted, the approval will be limited to specific indications. Our product candidates may not receive regulatory approvals for marketing, or if approved, that approval may not be for the indications that we requested.

Other regulatory agencies follow similar procedures to those required by the FDA and require that the safety and efficacy of our pharmaceutical product candidates be supported through adequate and well-controlled clinical trials. If the results of our pivotal clinical trials submitted in an application for approval do not establish the safety and efficacy of our product candidate to the satisfaction of any regulatory agency, we will not receive the approvals necessary to market our product candidate in that country.

In the European Union, or EU, the registration process for certain products can be done through a decentralized procedure. Under this procedure, the holder of a national marketing authorization for which mutual recognition is sought may submit an application to one or more member states, certify that the dossier is identical to that on which the first approval was based or explain any differences and certify that identical dossiers are being submitted to all member states from which recognition is sought. Within 90 days of receiving the application and assessment report, each member state must decide whether to recognize the approval. The procedure encourages member states to work with applicants and other regulatory authorities to resolve disputes concerning mutual recognition. If such disputes cannot be resolved within the 90-day period provided for review, the application will be subject to a binding arbitration procedure.

Following approval, regulatory agencies continue to regulate our approved and marketed products. We must report adverse drug events associated with our products to the regulatory agencies. In addition, the regulatory agencies also inspect on a regular basis the equipment and facilities used to manufacture our products. A regulatory agency may suspend the manufacturing facilities (and order a recall of our products manufactured in that facility) if the regulatory agency believes that the product has not been manufactured in compliance with regulations.

Employees

As of December 31, 2002, we employed 299 people worldwide, of which 110 are in the U.S. and Canada and 189 are in Europe, which includes approximately 74 employees in our manufacturing facility near Lyon, France. Most of our employees in our French facilities are represented by labor unions. We believe that we maintain good relations with our employees.

Available Information

Our Internet address is http://www.sangstat.com/. Information contained on our website is not part of this annual report on Form 10-K. We make available free of charge on http://www.sangstat.com/ our annual report on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Statements of changes in beneficial ownership of our securities on Form 4 by our executive officers and directors are made available on our web site by the end of the business day following the submission of such filings to the SEC.

In addition, you may request a copy of these filings (excluding exhibits) at no cost by writing or telephoning us at the following address or telephone number:

SangStat Medical Corporation
6300 Dumbarton Circle
Fremont, CA 94555
Attention: Investor Relations
Telephone: (800) 298-1738

Code of Ethics

We have adopted a Financial Code of Ethics for our chief executive officer, chief financial officer, controller and finance director, Europe. A copy of the Financial Code of Ethics is available on our web site at http://www.sangstat.com/. We intend to post on our web site any material changes to, or waiver from our code of business conduct, if any, within five business days of such event.

Risk Factors

We have a history of operating losses, and our continued profitability is uncertain.

We were incorporated in 1988 and have experienced significant operating losses since that date. As of December 31, 2002, our accumulated deficit was $180.7 million. While the 2002 year was a profitable year, we may recognize losses in subsequent periods for a variety of reasons, particularly if we are unable to sell Gengraf in the future or if we increase our research and development expenditures directly or through investment or partnering arrangements with others. We expect to continue the development of our existing products and to enter into license or partnering arrangements in the future.

To date, our product revenues have been primarily derived from sales of Thymoglobulin, Lymphoglobuline, and Gengraf. Revenues from Thymoglobulin were 60%, 54% and 58% of total revenues in 2000, 2001 and 2002, respectively. Revenues from Lymphoglobuline were 12%, 8% and 7% of total revenues in 2000, 2001 and 2002, respectively. In addition, revenues from Gengraf were 18%, 31% and 31% of total revenues in 2000, 2001 and 2002, respectively. If Abbott were required to obtain a license from Novartis to continue the sale of Gengraf, Abbott s cost of sales for Gengraf may increase, and Gengraf sales may fall dramatically if this increased cost renders Gengraf less competitive in the marketplace. We believe that under our agreement with Abbott, any royalties due to Novartis should be paid by Abbott solely from Abbott s share of Gengraf profits, but Abbott may contest this. If Gengraf were withdrawn from the market due to the Novartis patent lawsuit against Abbott, these revenues would be lost entirely.

While we experienced our first profitable year in 2002, we may not be able to maintain or increase our financial reporting profitability on a quarterly or annual basis. Our operating results will be significantly dependent upon our success in, among other things:

maintaining and increasing revenues from Thymoglobulin, Lymphoglobuline and Gengraf, particularly Thymoglobulin;

Abbott s ability and willingness to continue marketing Gengraf despite the recent judgment that Gengraf infringes a Novartis patent;

successfully commercializing our product candidates, especially RDP58;

limiting our manufacturing and selling, general and administrative expenses; and

controlling research and development expenses.

Our operating results may also be affected by the licensing of complementary products or the investments in or acquisition of products or companies we may effect in the future. Any such acquisition or licensing could have the immediate effect of causing an operating loss in future periods. In this regard, our recent collaboration with and investment in Human Therapeutic Polyclonals decreased our level of profitability in 2002.

Fluctuations in quarterly and annual operating results may decrease our stock price.

Our quarterly and annual operating results may fluctuate due to a variety of factors, and these fluctuations may not match the expectations of investors and securities analysts. This could cause the trading price of our common stock to decline substantially. We therefore believe that quarter-to-quarter comparisons of our operating results may not be a good indication of our future performance, and you should not rely on them to predict our future performance or the future performance of our stock.

We also expect our operating results to fluctuate significantly as a result of a number of factors, including:

the uncertainty in the timing and the amount of revenue we earn upon product sales, including seasonal fluctuations;

our ability to continue marketing Gengraf in light of pending litigation between Novartis and Abbott and a judgment in favor of Novartis, and Abbott s willingness to continue marketing Gengraf;

our achievement of research and development milestones;

expenses we incur for product development, clinical trials and marketing and sales activities;

the licensing of new products or the acquisition of products or other companies;

increased competition by existing or new products;

regulatory action;

market acceptance of our products;

manufacturing capabilities;

cost of litigation; and

third-party reimbursement policies.

Fluctuations in our operating results have affected our stock price in the past and are likely to continue to do so in the future.

If our preclinical and clinical testing of potential products is unsuccessful, our business will be harmed.

Before obtaining regulatory approval for the sale of any of our product candidates, we must subject these product candidates to extensive preclinical and clinical testing to establish their safety and efficacy. If these tests are unsuccessful, we will be unable to commercialize these products. We expect to announce the results of our Phase II trials of RDP58 for patients with mild-to-moderate ulcerative colitis or Crohn s disease in the second quarter of 2003. As our lead and primary product in development, adverse or inconclusive results from these trials would have a significant and material adverse effect on our research and development program and our prospects. In any event, interim results of trials do not necessarily predict final results, and acceptable results in early trials may not be repeated in later trials. Success in preclinical testing and

early clinical trials does not ensure that later clinical trials will be successful. For example, we delayed our expected filing for our cyclosporine capsule by approximately six months due to unanticipated results on an initial clinical trial for that product, and we could experience further delays in the future for this and other products. Similarly, we recently announced preliminary results from our PhaseII/III study of ABX-CBL indicating that survival with ABX-CBL was similar to ATGAM. Based on these results, we do not plan to pursue further development of ABX-CBL. Moreover, preclinical and clinical data can be interpreted in different ways, which could delay, limit or prevent regulatory approval. Negative or inconclusive results or adverse medical events during a clinical trial could cause a clinical trial to be repeated or a program to be terminated. We typically rely on third-party clinical investigators to conduct our clinical trials and other third-party organizations to perform data collection and analysis and, as a result, we may face additional delaying factors outside our control. The rate of completion of clinical trials depends, in part, on the enrollment of patients, which in turn depends on many factors such as the size of the patient population, the proximity of target patients to clinical sites, the eligibility criteria for the trial, the trial design, perceived risks and benefits, availability of the study drug and the existence of competitive experimental or approved therapies. Any delay in planned patient enrollment in our current or future clinical trials may result in increased costs, trial delays or both. Our product development costs will increase if we have delays in testing or approval or if we need to perform more or larger clinical trials than planned. If the delays are significant, our financial results and the commercial prospects for our products will be harmed.

Our future growth depends on sales of key products.

We expect to derive most of our future revenues from sales of Thymoglobulin, Lymphoglobuline, and Gengraf. We have limited experience selling our products in the U.S. Our sales of Thymoglobulin began in the U.S. in February 1999. We began distributing Gengraf in May 2000. We are marketing Gengraf in the U.S. under a co-promotion agreement with Abbott Laboratories. Abbott could be required or could elect to discontinue or curtail marketing of Gengraf in light of the recent judgment that Gengraf infringes a Novartis patent.

Because we expect Thymoglobulin