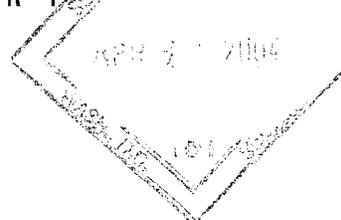


ARLS



Stressgen is pioneering innovative immunotherapeutics to treat viral diseases and cancers

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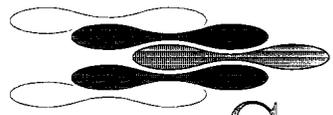


*Looking at drug development through the eyes of scientists, physicians and patients*

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Stressgen  
BIOTECHNOLOGIES  
CORP

# 2003 Highlights

In 2003, we set the foundation to build a commercial biotechnology company.

- **RECEIVED FAST TRACK DESIGNATION FROM THE FDA THAT COULD FACILITATE AN EFFICIENT REGULATORY REVIEW OF HSP E7 FOR RRP**  
We received U.S. Food and Drug Administration (FDA) approval for a Fast Track Product Development Program for our lead compound, HspE7, in the treatment of patients with recurrent respiratory papillomatosis (RRP). In addition to providing access to a number of FDA programs to enhance HspE7 development, the designation may help the compound be considered for priority review and accelerated approval. Sponsors of products in Fast Track Development programs are also eligible to submit "rolling Biologics Licensing Applications," enabling the FDA to commence review of portions of the application before the sponsor submits a complete application.
- **ANNOUNCED COMPELLING CLINICAL RESULTS WITH HSP E7 IN RRP**  
We released statistically significant results in our Phase II HspE7 clinical trial in patients with RRP. These results support a filing for regulatory approval, a key step on the path towards commercialization.
- **ENHANCED PARTICIPATION IN OUR ROCHE COLLABORATION**  
We restructured our 2002 collaboration with Roche to maximize the potential of our lead product, HspE7. The restructured alliance broadens the scope of the original agreement to provide for multiple indications to be developed in parallel, provides an effective route to market for HspE7, and creates significant value for Stressgen and our shareholders through increased revenues and downstream product rights.
- **IDENTIFIED STRONG MANUFACTURING PARTNER: AVECIA LIMITED**  
In tandem with our clinical efforts, we have taken steps to ensure we have the manufacturing capacity in place to support the maturing HspE7 development and commercialization programs.
- **STRENGTHENED FINANCIAL POSITION**  
We completed a C\$20 million financing and received milestones from Roche totaling US\$4.5 million. We enter 2004 with a strong balance sheet to support our development projects into 2005.
- **SECURED KEY INTELLECTUAL PROPERTY**  
We strengthened our intellectual property estate with the issuance of both a U.S. and European patent for HspE7. We filed additional patent applications directed to heat shock protein (Hsp) fusions with other viral antigens.

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— Viral Infections

— Immune System

— Heat Shock Proteins

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— Selected Financials and Forward Looking Statement

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The annual report contains forward-looking statements including discussions of our drug development plans, the therapeutic potential of our products, the possibility of regulatory approval and marketing, and potential revenue from collaborations. Please refer to page 18 regarding risks that could affect the actual outcomes.

**Stressgen is SEEKING TO IMPROVE HUMAN**

**HEALTH BY CREATING A NEW CLASS OF PROPRIETARY**

**IMMUNOTHERAPEUTICS, OR THERAPEUTIC VACCINES,**

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**THAT WILL HARNESS THE POWER OF THE IMMUNE**

**SYSTEM TO TREAT THE MILLIONS OF PATIENTS WITH**

**CHRONIC VIRAL DISEASES AND CANCER. —Daniel L. Kopolinski**

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# Stressgen is developing products that stimulate the body's own immune system to treat viral diseases and cancers

## HISTORICAL TIMELINE ON EVOLUTION OF VIRAL DRUG DEVELOPMENT

*Humans used the word "virus" to describe the kind of stench or poison that arose from swamps.*

**1796**

Jenner develops smallpox vaccine.

**1879-1886**

Pasteur develops rabies vaccine.

**1935**

Elling develops yellow fever vaccine; introduction for use in humans.

**1954-1955**

Salk and Sabin develop polio vaccines.

**1957**

Interferon discovered by Isaacs and Lindenmann.

**1970**

Polio vaccine introduced for use in humans.

**1977**

Smallpox is declared eradicated.

**1981**

Hepatitis B virus vaccine licensed for general use (13 years after studies initiated).

**1986**

First monoclonal antibody (Orthoclone OKT3) approved by FDA. Recombinant hepatitis B vaccine licensed (11 years after studies initiated).

**1991**

Intron A, first alpha interferon, is approved by the FDA to treat chronic hepatitis B and hepatitis C.

**2007**

First therapeutic vaccine for RRP.

# VIRAL INFECTIONS

Of the many infectious diseases that affect mankind, those spread by viruses cause significant morbidity and mortality. Many viral infections are able to evade detection by the immune system. This ability enables the viruses to persist in the body, triggering chronic symptoms, often for the life of the individual. Over time, viral infections can lead to debilitating and life-threatening medical conditions, including cancer or organ dysfunction and/or failure. In contrast to bacterial infections, where treatment with antibiotics historically has been highly effective, viral infections are often poorly treated by existing drugs. Viruses have also been shown to develop resistance to drugs in many cases. Preventative vaccines are available for some viral diseases, including measles, mumps and rubella, and are routinely given to infants and children. However, for such other widespread viruses as hepatitis C, human papillomavirus (HPV) and human immunodeficiency virus (HIV), no vaccines exist.

In many cases where anti-viral drugs are used, large segments of the population are not effectively treated. The lack of effective anti-viral drug therapies, combined with the ability of viruses to hide from the immune system, has left millions of individuals worldwide suffering from life-long viral infections. Stressgen is pioneering a therapeutic vaccine platform to trigger the immune system to detect and eradicate previously “hidden” virus-infected cells. This novel technology may offer an important solution to the growing worldwide healthcare crisis of viral infections.

# The immune system is the body's primary defense against infection by pathogens such as viruses, bacteria and parasites

*Stressgen is positioned at the forefront of therapeutic vaccine development and may be one of the first companies to successfully bring a new immunotherapeutic, or therapeutic vaccine, to market.*

Therapeutic vaccines are quite different from the preventative vaccines we are given as children or adults, such as polio or measles vaccines. Preventative vaccines prevent an infection from becoming established and are often designed to trigger antibody responses.

While preventative vaccines are highly effective, there are many serious diseases for which preventative vaccines do not exist or are not effective in all recipients. One of the primary reasons this situation exists today is the lack of approved vaccine technologies that can trigger cellular immunity safely and effectively.

**Therapeutic vaccines** are designed to induce cellular immunity, especially cytotoxic T lymphocyte (CTL)

responses, which can eradicate established disease. These cellular immune responses are capable of killing virus-infected or cancer cells and hence can treat established disease. CTL responses are precisely the type of immune responses triggered by Stressgen's proprietary CoVal™ fusion protein vaccines.

Stressgen's lead CoVal™ fusion protein product, HspE7, has been tested in Phase II and Phase III clinical trials as a therapeutic vaccine for treating diseases caused by human papillomavirus (HPV). HspE7 has the potential to be the first therapeutic vaccine approved for use in humans, opening the door to follow-on CoVal™ fusion protein products for many other serious viral infections and cancer.

# THE IMMUNE SYSTEM

<b>HUMORAL</b>	<b>CELLULAR</b>
prevents infection)	(fights established infections)
stimulates antibody production	stimulates CD4+ and CD8+ (killer T) cell production
eliminates extracellular bacteria, viruses and other foreign pathogens	clears intracellular pathogens, virus-infected cells and tumor cells

## CoVal™ Fusion Protein Therapeutics



**Stressgen is advancing a  
technology platform that has the potential  
to treat multiple disease targets**

An easy-to-understand animated representation of the CoVal™ fusion therapeutics mechanism of action can be viewed by inserting the disc at left into any computer.

The CD also contains a detailed summary of Stressgen's unique approach to targeting diseases, as well as a scientific tutorial, a scientific glossary, Stressgen's Annual Report on Form 10-K for the fiscal year ended December 31, 2003 and other important information.



Stressgen's fusion technology covalently links a heat shock protein (Hsp) – also known as a stress protein – to an antigen to create a single hybrid molecule. This technology is a platform from which a variety of Hsp fusions can be built, each specific for the treatment of a different disease.

# THE POWER OF HEAT SHOCK PROTEINS

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To create therapeutic vaccines, Stressgen takes advantage of the immunostimulatory powers of heat shock proteins (Hsp), also known as stress proteins.

Hsp are especially potent triggers for cellular immunity, including cytotoxic T lymphocytes (CTL). CTL, referred to as “killer T cells,” are peptide-specific white blood cells that can recognize and kill infected or cancerous cells, while bypassing normal cells. By stimulating the patients’ own immune system to recognize and eradicate infected cells, therapeutic vaccines may achieve cellular immunity and offer safe, more durable treatment options than currently available drugs.

Stressgen’s CoVal™ fusion protein products are composed of two parts: a stress protein and a protein antigen selected from a virus or cancer cell. The stress protein and antigen are joined or “fused” together *covalently* using recombinant DNA technology. Each CoVal™ fusion protein represents a new virus or cancer-specific therapeutic vaccine.

The protein antigen that Stressgen fuses to a heat shock protein can be chosen from a wide variety of sources. As a result, the spectrum of diseases that potentially can be treated by CoVal™ fusion immunotherapeutics ranges beyond viral diseases to other types of infections and cancer.

Stressgen is presently developing CoVal™ fusion immunotherapeutics for chronic viral infections with large unmet market and medical needs caused by human papillomavirus (HPV), and has initiated research studies to evaluate stress protein fusions for the treatment of hepatitis B and herpes simplex. In addition, the Company is targeting hepatitis C. The ability of CoVal™ fusion products to elicit a potent and targeted cellular immune response for a given disease may have extraordinary implications in the treatment of a wide range of diseases.

# CoVal™ Fusion Protein Therapeutics

*Stressgen is developing CoVal™ fusion products that elicit a potent and targeted cellular immune response for a given disease, with extraordinary implications in the treatment of a wide range of diseases.*

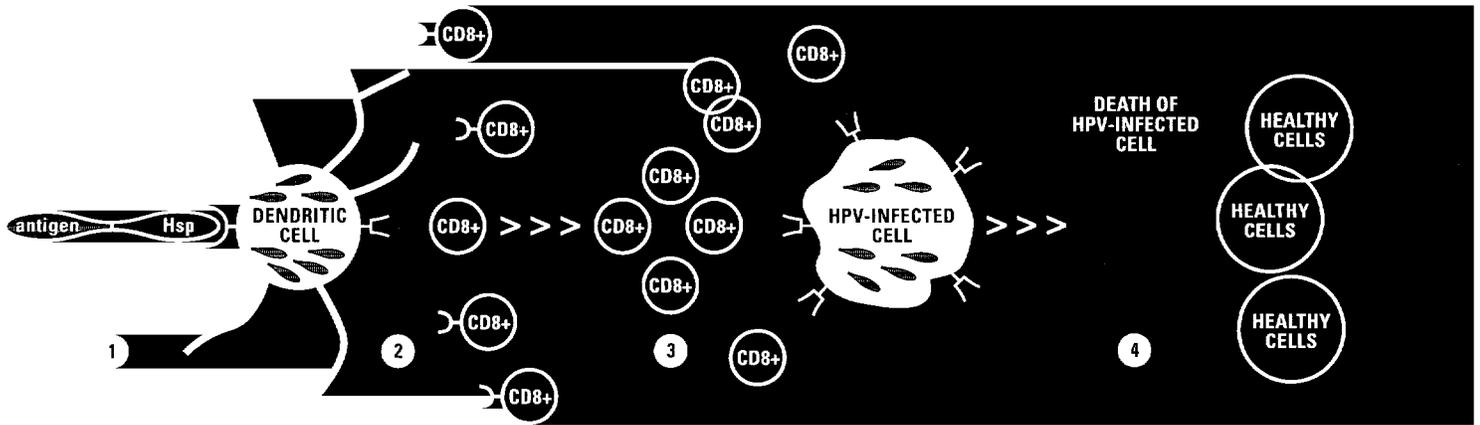
Stressgen's CoVal™ fusion proteins bring together the target specificity of viral or cancer cell antigens with the unique power of heat shock proteins (Hsp) (also known as stress proteins) to trigger effective immune responses. The Hsp provides heightened cellular immune responses; the antigen provides a specific target for CTL (killer T cell)-mediated destruction of infected or diseased tissues.

Hsp trigger immune responses by targeting dendritic cells (DCs), which are the primary activators of cellular immune responses. Stress proteins are able to trigger potent cellular immune responses, especially CTLs, because DCs possess receptors on their surface which bind to stress proteins. Hence, it is believed that immunization with CoVal™ fusion proteins directs the antigen portion of the fusion to DCs, which in turn trigger antigen-specific CD8+ CTLs. Therefore, CoVal™ fusion proteins may represent a new and highly effective way to stimulate killer T cell responses to viral and cancer antigens.

Stressgen's lead product, HspE7, is composed of the stress protein Hsp65 from a specific mycobacteria joined to the E7 protein antigen from human papillomavirus (HPV) type 16. Hsp65 was chosen based on abundant scientific evidence that it possessed strong immunostimulatory

powers. E7 was chosen because 1) it represents a precise target for an attack against HPV-infected cells in the body, 2) its expression is required to maintain infected cells in a transformed (cancerous) state, and 3) its protein sequence is similar in many types of HPV, which may permit induction of cross-reactive immunity against multiple HPV types. The HPV16 E7 antigen is expressed in many types of HPV infections, such as those that cause precancerous conditions called dysplasia, as well as in cancers associated with HPV. In many cases HPV16 E7 must be expressed for dysplastic and cancer cells to survive. As a result, a virus cannot "switch off" E7 expression to hide from the immune system. The constant expression of the antigen provides an advantageous target for the immune system to destroy infected cells displaying the E7 antigen on their surface.

HspE7 has shown activity in treating a variety of HPV-related conditions. To date, its safety profile has been favorable. In addition, HspE7 activity appears to be independent of CD4+ T helper cells, supporting the potential application of Hsp fusions in the treatment of immunocompromised patients whose CD4+ T helper cells may be depleted or significantly impaired.



**1 HSP FUSION PROTEIN**

The Hsp portion of the fusion protein activates a Type 1 (cellular) immune response. In the case of Stressgen's lead molecule, HspE7, the E7 portion generates an antigen-specific immune response, targeting the immune system to look for the E7 protein of HPV in infected cells.

**2 ANTIGEN PRESENTATION**

Hsp receptors on the cell surface enable the Hsp-antigen fusion to enter the dendritic cell. The fusion is processed into small pieces called peptides. Peptides from the E7 antigen are presented on the dendritic cell surface on Class I molecules for presentation to CD8+ T cells.

**3 CYTOTOXIC T LYMPHOCYTE (CTL) RESPONSE**

When CD8+ T cells encounter the E7 peptides presented by the dendritic cell, they become activated into CTLs, also known as "killer T cells." These E7-specific CTL proliferate and search the body for HPV-infected cells displaying the E7-antigen on their surface.

**4 TARGETED CELL DEATH**

Once the activated CTL locate these HPV-infected cells, the CTL kill the cells. Only the HPV-infected cells are destroyed, while healthy cells and tissues are spared.



**Stressgen is developing its lead product candidate, HspE7, to treat a variety of HPV-related diseases and cancers**

*HPV causes the most prevalent sexually transmitted diseases in the world. Approximately 20 million patients in the United States alone are currently infected with HPV, and 5.5 million new HPV infections are reported in the country each year.*

# MARKETING OPPORTUNITIES FOR HspE7

Stressgen has completed 11 trials with its lead product, HspE7, in patients with HPV-related diseases, including genital warts; recurrent respiratory papillomatosis (RRP), which occurs in babies born to mothers with HPV; and two pre-cancerous conditions, anal dysplasia and cervical dysplasia.

The focus of Stressgen's HspE7 development program has evolved to leverage the results from these clinical trials, ensure that the Company captures its broadest potential markets for the product, and capitalize on the resources of third parties interested in using HspE7 to treat specific indications. Because the compound has received Orphan Drug Status and Fast Track Product Development designations from the U.S. Food and Drug Administration (FDA) for the treatment of patients suffering from RRP, and based on Stressgen's comprehensive evaluations, the Company is targeting RRP as the first market for HspE7.

Stressgen has identified serious, unmet medical indications beyond RRP for which HspE7 might be beneficial. These include high-grade cervical dysplasia in women. The current "gold standard" therapy for this condition is a surgical procedure, known as LEEP (Loop Electrosurgical Excision Procedure), which is invasive, does not always work and can reduce fertility. Stressgen believes HspE7 could prove a viable and long-term alternative to surgery. Stressgen is also looking at ways to help HPV-infected patient groups whose immune systems are not functioning properly. These include those who are HIV-positive, have received organ transplants or are elderly.

As with RRP, the above indications represent attractive potential commercial opportunities. They may require smaller clinical trials and may qualify for Orphan Drug Status and Fast Track Product Development program designations by the FDA. Stressgen is actively evaluating potential clinical development activities in these areas and await valuable dysplasia data from two ongoing studies – an investigator study and a National Cancer Institute (NCI) trial – which may be available by the fourth quarter of 2004.

## Human Papillomavirus (HPV) Indications

**GENITAL WARTS** are caused by certain types of sexually transmitted HPV. Approximately two-thirds of people who have sexual contact with a partner who has genital warts develop warts themselves, usually within three months of contact. An estimated 500,000 to 1 million new cases occur in the United States each year and while the lesions may spontaneously regress, recurrence is typical even following treatment.

Stressgen's current agreement with Roche provides exclusive and global rights to Roche to develop a 2nd generation HspE7 compound for genital warts.

**RECURRENT RESPIRATORY PAPILLOMATOSIS (RRP)**, a disease caused by the same types of HPV that cause genital warts, occurs primarily on the larynx and vocal cords of children born to mothers infected with HPV. The papillomas, or warts, occasionally spread into the trachea and lungs. Based on a 1995 survey estimating over 2,000 new cases of pediatric RRP and 3,500 new cases of adult RRP

each year in the United States there would be approximately 17,200 patients in the United States. Patients with RRP can die from airway obstruction, cancerous transformation, overwhelming spread of the disease, growth of papillomas in the lungs or complications of surgical treatments. Pediatric patients tend to have about five surgeries per year, and some children have hundreds of procedures during their lifetime. There are no drugs or immunotherapies approved for RRP in the United States. Stressgen is focusing its development resources and efforts on RRP.

**CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN)**, also known as cervical dysplasia, is characterized by abnormal cells in the cervix associated with the malignant transformation of epithelial cells infected with HPV virus. Annually, in the United States more than 1.2 million women are diagnosed with low-grade cervical dysplasia and another 200,000 to 300,000 are diagnosed with high-grade cervical dysplasia in the United States. Worldwide, the problem is much larger.

*approximately one-third infecting genital epithelial tissue and primarily spread through sexual contact. Low-risk types of HPV typically cause skin warts, the most recognizable sign of genital HPV infection. Other high-risk types of HPV cause cervical and anal dysplasia, which are precursors to cervical and anal cancer.*

200,000 to 300,000 are diagnosed with high-grade cervical dysplasia in the United States. Worldwide, the problem is much larger.

CIN often precedes cervical cancer, a worldwide public health problem particularly in countries where routine Pap smears are not practiced. American Cancer Society estimates for 2002 predicted that approximately 13,000 women in the United States would be diagnosed and about 4,100 would die from invasive cervical cancer. Globally there are approximately 500,000 new cases of cervical cancer identified each year, resulting in nearly 300,000 deaths. Although death rates from the disease have declined, invasive cervical cancer continues to be associated with extreme morbidity.

The current treatment for CIN involves local surgical techniques, which may not remove all dysplastic cells and do not treat underlying viral infection. In addition, surgery can result in complications such as reduced fertility.

**ANAL INTRAEPITHELIAL NEOPLASIA (AIN)**, or anal dysplasia, is characterized by the presence of abnormal cells that may precede anal cancer. Data extrapolated from studies of homosexual and bisexual men and the anal cancer population suggests that there may be 500,000 new cases per year in the United States. Patients are not commonly screened for AIN; however, there is increasing awareness of the condition. No standard therapy exists for AIN.

The U.S. National Cancer Institute (NCI), recognizing the potential of HspE7 to prevent cancers caused by HPV, is sponsoring several clinical trials using the compound in cervical dysplasia and immunocompromised HIV-positive anal dysplasia patients. Data from these trials will help Stressgen plan its next steps in developing HspE7 for cervical and/or anal dysplasia.

# Stressgen is making and seizing on opportunities to bring its innovative immunotherapies to market



## *To Our Shareholders:*

In 2003, Stressgen made significant strides in several key areas of our growth, including targeting and advancing our clinical development efforts of our lead compound, HspE7, for the treatment of HPV-related diseases; expanding our product development collaboration with Roche; increasing our breadth of

process development and manufacturing capabilities and building our financial strength. We have leveraged opportunities on multiple fronts to ensure that we have the capabilities and resources to drive the clinical development of HspE7's first indication to the marketplace as quickly as possible for the treatment of recurrent respiratory papillomatosis (RRP).

RRP, one of several severe diseases caused by the human papillomavirus (HPV), strikes both children and adults. Current treatment involves multiple surgical interventions over the lifetime of patients. Data from our completed Phase II RRP clinical trial confirmed the potential for HspE7 to significantly reduce the number of surgeries for the children participating in the study. We look to HspE7 to be an important addition to a physician's armamentarium to manage patients suffering from RRP, and a host of other serious diseases caused by HPV, including infections in 1) HIV-positive immunosuppressed patients with concomitant HPV disease, 2) women with serious high-grade cervical dysplasia who fail LEEP (Loop Electrosurgical Excision Procedure) surgery, and 3) patients with HPV-related cancers such as cervical, anal and approximately one-third of head and neck cancers. Even excluding other HPV-related diseases, HPV causes disease symptoms in over 1 million new genital warts patients in the United States.

We believe that HspE7 has the potential to be a front-runner in a totally new class of drugs, therapeutic vaccines, to treat viral diseases and cancer by mobilizing the immune system to target diseased cells. Successful commercialization of HspE7 could provide a major

advance in the management of HPV-related diseases. With the introduction of HspE7, we believe our Company and our shareholders can make a major contribution to the treatment of HPV-related diseases.

## **ADVANCING HSPE7 IN CLINICAL DEVELOPMENT**

Over the recent past and in 2003, we gathered increasing clinical evidence to support our belief that HspE7 will treat multiple diseases caused by HPV, including genital warts, RRP, cervical dysplasia, anal dysplasia and various cancers.

We recently completed an open-label Phase II trial in 27 pediatric patients with RRP who required frequent and painful surgery for their papillomas. Treatment with HspE7 increased the time interval between required RRP surgeries and thereby reducing the frequency of surgery in patients with moderate and severe RRP. In fact, the median interval of all surgeries reported following treatment suggests that the 27 children treated in the trial would experience 87 fewer surgeries during the first year post-treatment. Most significantly, the high level of statistical significance in a small population and the internal consistency of the RRP data according to a variety of measures suggest that results to be obtained in a carefully designed pivotal trial are likely to be robust and reproducible. These extremely ill children with RRP have to repeatedly undergo surgeries under anesthesia. A reduction in the number of these procedures will be a welcome benefit for the children, their caregivers and the physicians who treat them.

Stressgen has been granted Orphan Drug Status and Fast Track Product Development designations from the U.S. Food and Drug Administration (FDA) for HspE7 in the treatment of patients suffering from RRP. Based on our findings from the clinical trials conducted to date, advice from an ad hoc clinical advisory board, market research and our experience with the regulatory approval process, Stressgen is targeting RRP as the first market for HspE7. We plan to begin a pivotal RRP trial with HspE7 and anticipate submitting a Biologics License Application (BLA) for the indication in mid-2007.

We also recently completed our Phase III anal dysplasia trial in which HspE7 was used to treat high-grade anal dysplasia patients, a precursor to anal cancer. This trial was designed to test the proposition that HspE7 produces a pathological response rate superior to placebo in anal dysplasia. In addition, this trial was designed to evaluate the proposition that an adjudicated read of pathological assessment would be a viable primary endpoint in a pivotal Phase III trial. This trial was not intended to be a pivotal trial.

The final analysis showed that the drug exceeded the treatment effect that it was intended to detect. However, the anticipated placebo effect doubled as estimated from previous Phase II trials and as had been predicted by experts through studies of natural history, and thus there was no difference between drug and placebo. The 28 percent discordance in the adjudicated pathological assessment of biopsies makes it very difficult to interpret these results.

Nonetheless, HspE7 reproduced Phase II results in the secondary endpoint of Physician's Global Assessment (PGA). PGA, a blinded assessment, represents a scoring by the treating physician of overall patient outcomes and takes into account variables such as extent and depth of disease as well as pathological analysis of biopsies. PGA reached statistical significance for anal dysplasia at six months with 80 percent of patients showing improvement. These results were in line with PGA responses in the previous Phase II anal dysplasia study. In the additional secondary endpoint measuring global assessment in the patients with concomitant genital warts, HspE7 demonstrated an increasing treatment advantage and became statistically significant at 48 weeks. These results are consistent with the beneficial effect in genital warts observed in previous Phase II studies, i.e., 80 percent complete responses at 48 weeks. Finally, patients in this Phase III study were followed up to 24 months and 73 percent who achieved complete remission were in complete remission at the end of the study. Similarly, 70 percent of the complete responders in our Phase II study were in complete remission at the 24 month observation point.

#### **ENHANCING VALUE THROUGH OUR COLLABORATIONS**

During 2003, we broadened and restructured our HspE7 collaboration with our partner Roche. This restructuring was designed to increase the potential of revenue flowing into Stressgen, to broaden HPV disease targets, to equal-

ize resource allocation by both companies, and to take advantage of Stressgen's experience to lead the clinical development of HspE7 down a faster commercialization pathway. In our new agreement, Stressgen will develop the current 1st generation HspE7, now in clinical trials, for all HPV indications except genital warts. Roche has the right to independently develop a 2nd generation technology – one with a unique and separate HspE7 formulation – to treat genital warts. This new structure allows full utilization of each company's expertise and resources to develop HspE7 for multiple indications on parallel tracks.

Assuming that all HspE7 development and commercial milestones are achieved and Roche exercises its rights to certain other CoVal™ fusion product candidates, the payments to Stressgen, excluding royalty payments or sales-based payments, will be US\$227 million, in addition to the US\$21.5 million received from Roche to date. Potential payments of up to US\$15 million may be provided to us in 2005. We believe this restructured agreement adds significant value to our business. In the agreement, Stressgen captures top line revenue for three years from product sales in the United States and Canada, starting with the first U.S. BLA approval. In year four, Stressgen will receive significant royalty streams in both the United States and the rest of the world. These new terms provide a major advance in potential revenue streams and royalties, or sales-based payments, compared to our original agreement signed in June 2002.

In another collaboration, we have two clinical trial agreements with the U.S. National Cancer Institute (NCI) for the co-development of HspE7 for the treatment of dysplasia and cancer. Under the agreements, Stressgen provides clinical-grade supplies of HspE7 and is able to use any resulting trial data. The NCI's support includes creating a general development plan, soliciting research protocols, recruiting investigators and funding the trials. The collaboration with the NCI enables studies of HspE7 for the treatment of dysplasias and pre-cancerous lesions to progress, while Stressgen uses its resources to advance RRP.

Two trials now underway may provide sufficient Phase II data to support pivotal Phase III trials for HspE7 in HIV-positive immunosuppressed patients with concomitant HPV infection, and for women with serious high-grade cervical dysplasia who fail LEEP surgery. Successful pivotal trials could see new label indications for these serious HPV-related diseases.

#### **INCREASING OUR MANUFACTURING CAPABILITIES**

To better utilize resources of both partners, Stressgen has reacquired control of the manufacturing process, for both clinical trial supplies and commercial product, for the 1st generation HspE7 therapeutic vaccine now in advanced clinical trials. Under the current agreement, Roche has responsibility for the manufacture of 2nd generation HspE7 for genital warts. To meet our BLA filing target, we have contracted Avecia Limited to complete development of the commercial process and provide clinical supplies for our Phase III RRP, and other HspE7 clinical trials. Avecia's management and experience in the scale-up of biologics, coupled with its modern manufacturing facility to meet the market needs for commercial products, gives us confidence that we will meet the Company's target for marketing HspE7. The program is on schedule, and we have already developed and validated a bioassay for the release testing of HspE7, a major step in the manufacturing process. Similar to our restructured agreement with Roche, the Avecia contract demonstrates management's ability to work with collaborators and to search for better ways to keep Stressgen's development program on track. Finally, commercial-grade material available from Avecia will produce clinical supplies for multiple Phase III trials for other indications, as well as drug for the market if HspE7 is approved for sale.

#### **BUILDING FISCAL STRENGTH THROUGH FINANCING AND BIOREAGENTS**

We enter 2004 with the financial resources to aggressively fund our development programs into 2005. The strength of our balance sheet is due in part to US\$4.5 million paid in 2003 from Roche as an equity investment and a development milestone payment, an aggregate US\$17 million paid by Roche in development work under our original collaboration, and a C\$20 million equity financing we completed in December 2003. These dollars, coupled with an average C\$2 million per year contribution from our bioreagent business, and a potential US\$15 million from Roche in 2005 from our newly restructured Roche partnership, lead us to believe that we will be able to maintain a solid financial picture as we move forward in the development of HspE7 and of our CoVal™ technology platform.

Despite downward pressure that the challenging economic environment presented, our bioreagent business remained profitable in 2003. Both our U.S. and Canadian dollar denominated sales increased by 4 and 10 percent respectively, aided by the introduction of several higher priced, kit-based research products. The weakening U.S.

dollar was the principal reason reported bioreagent sales were 6 percent lower in 2003 compared to 2002. We continue to view the bioreagent business as an asset and a source of cash for our therapeutic development business. With a strengthening economy, we expect the business can be grown through new product introductions or developed to attract capital from strategic partners.

#### **DEMONSTRATED MULTIPLE PRODUCT POTENTIAL OF COVAL™ FUSION PRODUCTS AND TECHNOLOGY PLATFORM**

HspE7 represents one of several potential commercial products that can be developed utilizing our proprietary technology platform. In 2003, we announced progress with our CoVal™ fusion protein for hepatitis B known as HspBcor. Repeatedly, HspBcor has been able to overcome tolerance in hepatitis B-infected transgenic mice by eliciting a specific CTL response, an observation critical for moving our HspBcor program forward towards clinical development.

Our successes with HspE7 and our preclinical studies with HspBcor suggest that the immunotherapeutics we create by covalently linking a heat shock protein to an antigen are effective in stimulating the immune system to recognize the specific-linked antigen and fight the disease. Our technology platform will potentially provide multiple CoVal™ fusion products to treat a variety of unmet medical needs in viral infections such as herpes simplex, hepatitis B and hepatitis C, and cancer. HspE7 for HPV infection represents the first in a family of products utilizing this novel proprietary technology.

#### **VALUING YOUR SUPPORT**

The progress we made this year would not have been possible without the hard work and dedication of everyone at and connected with Stressgen. As such, I would like to thank my colleagues for their continued commitment toward advancing our first therapeutic to market. I also thank our directors for their guidance and leadership, and our shareholders, who have continued to support us throughout the year. On behalf of the Board of Directors, thank you all. I look forward to shaping and sharing Stressgen's continuing accomplishments with you.

Sincerely,



Daniel L. Kopolinski  
*Director, President and Chief Executive Officer*  
March 4, 2004

# PRODUCT PIPELINE

Product	Development Status						
	Under Consideration	R&D/ Discovery	Pre-Clinical	Phase I	Phase II	Phase III	Market
<b>CoVal™ Fusion Products</b>							
HspE7							
Recurrent Respiratory Papillomatosis (Orphan Drug & Fast Track Status)							
Genital Warts							
HIV+ Anal Dysplasia							
Cervical Dysplasia (HSIL)							
Anal Dysplasia (HSIL)							
Cervical Cancer							
Head & Neck Cancer							
<b>HEP B-COR</b>							
Hepatitis B							
<b>HEP C ANTIGEN</b>							
Hepatitis C							
<b>HSV ANTIGEN</b>							
Herpes Simplex Virus							
<b>Business Opportunities Under Consideration to Supplement Pipeline</b>							
In-licensing Complementary Product							
Later-Stage							
Early-Stage							
In-licensing New Technology Platforms							
Mergers & Acquisitions Activities, Joint Ventures or Collaborations							

HSIL: High-grade squamous intraepithelial lesions – precursors to cervical and anal cancers.

## Disease Targets

Stressgen is developing a preclinical pipeline of CoVal™ fusion proteins for other large market viral infections. It is concentrating its early-stage research efforts on the treatment of hepatitis B and herpes simplex viruses, and is evaluating the use of its technology to develop a fusion protein to treat infections caused by hepatitis C virus. Treatments for cancer, bacterial and fungal diseases are possibilities for future development.

### HPV-RELATED DISEASES AND CANCERS

Current estimates of the costs of genital HPV-related diseases make HPV the second most costly sexually transmitted disease after HIV infection. HspE7 has the potential to reduce or eliminate recurrence and treat chronic conditions in people already infected with HPV.

### HEPATITIS B VIRUS (HBV)

Although safe and effective preventative vaccines exist for HBV, the United States has an estimated 1 million to 1.25 million cases of chronic HBV; between 140,000 and 320,000 new cases each year; and an estimated 4,000 to 5,000 HBV-related deaths annually. Worldwide, about 1 million deaths are attributable to HBV each year. Due to the large infected population and small percentage of the public being vaccinated for the disease, the need for new and effective therapies for chronic HBV infection remains great.

### HEPATITIS C VIRUS (HCV)

HCV infects an estimated 200 million people worldwide and 3.9 million people in the United States (1.8 percent of the population), with 8,000 to 10,000 U.S. deaths attributed to HCV annually. Researchers predict that over the next 10 to 20 years, chronic HCV infection will become a major burden on the health care system as patients progress to end-stage liver disease. Currently there is no vaccine or available therapy to eradicate the virus or do more than delay the progression of the disease.

### HERPES SIMPLEX VIRUS (HSV)

The cause of genital herpes, HSV-2, is now detectable in about one in five persons 12 years of age or older in the United States. An estimated 45 million Americans are already infected with genital herpes, with an additional 500,000 to 1 million new cases estimated to occur each year. Except in newborns, genital herpes is not life threatening. Nonetheless, it is distressing and can contribute to the spread of other sexually transmitted diseases.

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## **Note Regarding Forward-Looking Statements**

The forward-looking statements in this annual report involve risks and uncertainties, including the discussions of collaborations, revenue, product development efforts and the future of our products. Actual results may differ materially from our current expectations due to factors including uncertainties associated with the development of therapeutics, the risk that we will not obtain regulatory approval for our products and our need for additional financing. Please see our Annual Report on Form 10-K, which is included on the enclosed CD-ROM and is available from our Investor Relations department, for a more detailed discussion of these and other risks.

## Selected Consolidated Financial Data

The following table summarizes certain selected consolidated financial data for each of the five years in the period ended December 31, 2003. The information presented is not necessarily indicative of the results of future operations and should be read in conjunction with the consolidated financial statements and related notes thereto and with "Management's Discussion and Analysis of Financial Condition and Results of Operations," included in the Company's 2003 Annual Report on Form 10-K. Our consolidated results include those of our subsidiaries, including a U.S. subsidiary, which provides management, research and development services, and a Barbados subsidiary, which is responsible for HspE7 development.

### Consolidated Statement of Operations Data

*(In thousands of Canadian dollars, except per share amounts)*

Year ended December 31	2003	2002	2001	2000	1999
Net revenues					
Canadian and U.S. GAAP	\$ 13,419	\$ 14,042	\$ 5,419	\$ 4,156	\$ 3,274
Research and development expenses					
Canadian and U.S. GAAP	20,865	33,675	35,906	23,961	14,322
Net loss					
Canadian GAAP	(16,245)	(28,802)	(35,939)	(25,407)	(16,738)
U.S. GAAP	(15,298)	(28,922)	(36,341)	(35,766)	(19,515)
Basic and diluted loss per common share					
Canadian GAAP	(0.26)	(0.49)	(0.70)	(0.63)	(0.58)
U.S. GAAP	(0.25)	(0.49)	(0.71)	(0.88)	(0.67)

### Consolidated Balance Sheet Data

*(In thousands of Canadian dollars)*

As of December 31	2003	2002	2001	2000	1999
Cash and short-term investments					
Canadian GAAP	\$ 52,090	\$ 46,013	\$ 62,682	\$ 70,567	\$ 16,477
U.S. GAAP	52,090	46,013	62,682	70,710	16,477
Total assets					
Canadian GAAP	56,430	54,815	67,789	74,325	19,852
U.S. GAAP	56,430	54,815	67,789	74,468	19,852
Long-term obligations					
Canadian GAAP	2,672	3,606	578	1,036	1,467
U.S. GAAP	2,672	3,606	578	1,036	1,467

# Corporate Information

## Corporate Governance

Management and the Board of Directors believe that Stressgen's corporate governance practices are in line with those established by The Toronto Stock Exchange. The mandate of the Board of Directors is to provide advice and guidance to the management of the Company and represent the best interest of shareholders. The directors are kept informed of the Company's operations at meetings of the board, its committees and through reports and analysis by management.

## Stock Listing

The Company's common shares are traded on The Toronto Stock Exchange under the symbol "SSB."

## Annual General Meeting

The Annual General Meeting of Shareholders will be held on Wednesday, May 12, 2004, at 1:00 p.m. at the Pan Pacific Hotel in Vancouver, British Columbia.

## Independent Auditors

Deloitte & Touche LLP  
San Diego, CA

## Transfer Agent and Share Registrar

Computershare Trust Company of Canada  
Computershare  
510 Burrard Street  
Vancouver, British Columbia V6C 3B9  
Telephone (Investor Services): 1-800-564-6253

## Shareholder Inquiries

For further information about the Company and its activities, please refer to the U.S. Annual Report on Form 10-K, available on the accompanying CD-ROM or through [www.sec.gov](http://www.sec.gov) or the Canadian Annual Information Form, available through [www.sedar.com](http://www.sedar.com).

Alternatively, please contact:

Stressgen Biotechnologies Corporation  
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Victoria, British Columbia V8Z 4B9  
Canada  
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Internet Site: [www.stressgen.com](http://www.stressgen.com)  
Email: [ir@stressgen.com](mailto:ir@stressgen.com)

## Corporate Profile

Stressgen Biotechnologies Corporation (TSX:SSB) is a public biopharmaceutical company focused on the discovery, development, and commercialization of innovative, proprietary immunotherapeutics for the treatment of infectious disease and cancer. The Company's proprietary platform technology is based on the covalent bonding of a stress protein, also called a heat shock protein (Hsp), to proteins such as viral or cancer antigens. The resulting CoVal™ fusion proteins are designed to stimulate immune responses to the disease-specific antigen present in the fusion. By targeting immune responses to a specific antigen, CoVal™ fusion proteins use the body's immune system to combat infectious diseases or cancer.

Stressgen recently completed a Phase II trial with HspE7, its lead product candidate, to treat children with a serious disease called recurrent respiratory papillomatosis (RRP) caused by the same HPV types, 6 and 11, that cause genital warts. The data from this trial were highly statistically significant, supporting the Company's decision to initiate a pivotal Phase III trial in RRP patients. HspE7 may also have applications in other indications caused by HPV, including genital warts, cervical dysplasia, cervical cancer and anal dysplasia. The U.S. Food and Drug Administration has granted Orphan Drug Status and designated HspE7 as a Fast Track Product Development program for the treatment of patients suffering from RRP. Stressgen is evaluating other CoVal™ fusion candidates for the treatment of viral infections caused by hepatitis B and herpes simplex viruses, and is targeting hepatitis C.

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U.S. SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20594

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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, 2003

Commission File No. 333-12570

**STRESSGEN BIOTECHNOLOGIES CORPORATION**

(Exact Name of Registrant as Specified in its Charter)

**Yukon Territory, Canada**

(State or Other Jurisdiction of Incorporation or Organization)

N/A

(IRS Employer Identification No.)

350-4243 Glanford Avenue  
Victoria, British Columbia V8Z 4B9

**Parent of Stressgen Biotechnologies, Inc.**

**6055 Lusk Boulevard, San Diego, California**

(Address of Principal Executive Offices)

**92121**

(Zip Code)

Registrant's Telephone Number, including area code: (250) 744-2811

**(858) 202-4900**

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

Securities Registered pursuant to Section 12(g) of the Act: **None**

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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 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 the 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

As of June 30, 2003 and February 12, 2004, the common shares held by non-affiliates of the Registrant had an aggregate market value of approximately U.S. \$77,830,916 and \$95,621,515, respectively. These amounts respectively represented approximately Cdn. \$105,484,240 (based on the June 30, 2003 closing price of Cdn. \$1.71 per common share, as reported on The Toronto Stock Exchange, and 61,686,690 outstanding common shares) and \$126,134,340 (based on the February 12, 2004 closing price of Cdn. \$1.74 per common shares as reported on The Toronto Stock Exchange and approximately 72,491,000 outstanding common shares). These numbers are provided only for the purposes of this report and do not represent an admission by either the Registrant or any non-affiliate as to the status of any person.

The Company's accounts are maintained in Canadian dollars. In this Annual Report on Form 10-K, all dollar amounts are stated in Canadian dollars except where otherwise indicated.

Documents incorporated by reference: None.

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## PART I

### FORWARD-LOOKING STATEMENTS

**This Annual Report on Form 10-K contains forward-looking statements that involve risks and uncertainties. Our forward-looking statements, which are typically indicated by words such as "intend," "plan," "anticipate" and "expect," include statements regarding the results of on-going research, development efforts and the scope of future operations. Such statements are only predictions. Actual results may differ materially from those implied by our forward-looking statements, due to factors including uncertainties associated with product development, the risk that products do not demonstrate statistically significant results in clinical trials, our dependence upon collaborative partners, our need for additional financing and the risk that we will not obtain approval to market our products. These and other risks are discussed in this Form 10-K, including under the caption "Factors that May Affect Future Performance." We disclaim any obligation to update forward-looking statements as circumstances change.**

#### Item 1. BUSINESS

##### Overview

We are a biopharmaceutical company focused on the commercialization, development and research of proprietary immunotherapeutics to treat human diseases. Our platform technology involves using recombinant DNA methods to covalently link together heat shock proteins (Hsp), also known as stress proteins, to proteins such as viral or cancer antigens. The resulting CoVal™ fusion proteins are designed to stimulate immune responses to the disease-specific antigen present in the fusion. By targeting immune responses to a specific antigen, CoVal™ fusions use the body's immune system to combat infectious diseases or cancer.

Most of our resources are devoted to developing our lead product candidate, which we call HspE7. HspE7 is a fusion between an Hsp and a human papillomavirus (HPV) antigen called E7. The product is in development for indications caused by HPV such as genital warts, recurrent respiratory papillomatosis (RRP), cervical intraepithelial neoplasia (CIN), cervical cancer and anal intraepithelial neoplasia (AIN).

If HspE7 is approved, it could be useful to treat a large number of patients and a broad spectrum of HPV diseases. There are approximately 5.5 million new genital HPV infections each year; more than 20 million people in the U.S. are currently infected with the virus. An analysis of healthcare costs associated with sexually transmitted diseases showed that the costs of HPV-related diseases ranked second only to the costs of HIV. HspE7 has the potential to reduce or eliminate recurrence and treat chronic conditions in people already infected with HPV.

HspE7 is important not only as a potential treatment for HPV-related indications but also as a demonstration of the efficacy of CoVal™ fusions. We believe that clinical results will show that fusions developed with our proprietary technology safely and effectively stimulate the immune

system to recognize and fight specific diseases. The type of immune responses induced by CoVal™ fusions, as demonstrated in preclinical research, indicates that the Hsp fusion platform technology may apply to the immunotherapy of a wide spectrum of diseases, including cancer and bacterial, fungal and parasitic infections. Robust preclinical and encouraging clinical data from the HspE7 program have led us to concentrate our current efforts on the treatment of viral diseases. We are performing research studies on potential treatments for hepatitis B (HBV) and herpes simplex and are evaluating the use of our technology to develop a fusion protein to treat infections caused by hepatitis C (HCV).

In addition to our biopharmaceutical business, we have a profitable bioreagent business. We supply stress proteins, antibodies and other bioreagents globally for use in academic, medical and commercial research. The production and sale of bioreagents enhances our business strategy by building a market presence in stress proteins and strengthening strategic relationships with other companies, academic institutions and stress response researchers.

### **Business Strategy**

Our business objective is to be a leader in the development and commercialization of novel immunotherapeutics for the treatment of virally-induced human disease. Our strategy includes the following elements:

- *Commercialize HspE7.* We intend to commercialize our lead product, HspE7 for the treatment of conditions caused by HPV.
- *Develop Candidates to Treat Additional Disease Targets.* We plan to develop promising CoVal™ fusion product candidates for the treatment of additional viral diseases, alone or with corporate partners.
- *In-License Synergistic Products.* We seek to strengthen our pipeline by in-licensing drug candidates that will complement our product line.
- *Use Our Core Competencies to Build Our Bioreagent Business.* By producing and selling compounds used in biotechnology research, we will generate revenue, build our market presence, further our relationship with stress response researchers, and capitalize on strategic opportunities for product discovery and development.

### **Scientific Overview**

Our technology uses Hsp covalently fused to antigens to activate the immune system.

#### ***The Immune System***

The human immune system is the body's natural defense mechanism to prevent and combat disease. The immune system protects the body by specifically recognizing and destroying invading viruses, bacteria and other pathogens. In addition, the immune system is capable of

recognizing and eliminating abnormal cells from the body, such as cells infected with viruses and to some degree precancerous and cancerous cells.

Scientists currently describe the human immune system as using two complementary mechanisms to respond to pathogens, labeled innate and adaptive immunity. Innate immunity, which is a "front-line" defense, includes dendritic cells, macrophages, natural killer cells and gamma delta T cells. These cells typically recognize structural components, including antigens, common to disease-causing organisms and generate a prompt, but relatively non-specific response. Adaptive or acquired immunity, which can be triggered by an innate immune response or operate independently, involves B cells and T cells. Adaptive immunity generates a "tailor-made" or antigen-specific response.

B cells make antibodies that prevent infection by attaching to invading pathogens and aiding in their disposal before they can infect cells. T cell responses are useful not only for helping antibody production, but also for eradicating existing infected or diseased cells. These two types of immune defenses are called humoral (B cell) and cellular (T cell) immunity. While both types of immune defenses may cooperate to defend against infection, scientists believe that once infection has been established, cellular immunity is required to eradicate such diseased cells.

Induction of a cellular immune response begins with the processing and presentation of antigens by specialized immune system cells called antigen presenting cells, such as dendritic cells. Once inside dendritic cells, protein antigens are broken down into small fragments, called peptides. These peptides are then presented on the dendritic cell surface. T cells continually scan the surface of dendritic cells for these peptides. When T cells recognize displayed peptides as being foreign, they replicate rapidly and then search for and kill diseased cells displaying those same peptides on their surface.

Peptides are presented to T cells through two distinct pathways designated as the class I and class II pathways. Presentation of such peptides by the class I and class II pathways activate different T cell subsets referred to as CD8+ T cells and CD4+ T cells. CD4+ T cells, which are also known as T helper (Th) cells, are further subdivided into Th1 and Th2 cells. Activated Th1 and Th2 cells release molecules known as cytokines, which trigger other immune cells to produce either a predominantly cellular (Th1) or antibody-mediated (Th2) immune response. Immune responses mediated by the cellular side of the immune system are characterized by the induction of CD8+ T cells called cytotoxic T lymphocytes (CTLs) or killer T-cells. Killer T cells are capable of directly killing pathogen-infected cells and cancerous cells.

### *Stress or Heat Shock Proteins*

Hsp are present in cells of all organisms from bacteria to mammals. The structure and function of Hsp are similar across these diverse life forms. Hsp play a major role in the generation of immune responses and appear to activate both innate and adaptive immunity. Some scientists refer to Hsp as molecular chaperones due to their role in transporting peptides within intracellular compartments. Hsp appear to activate both innate and adaptive immunity by interacting with newly identified Hsp receptors on antigen presenting cells such as dendritic cells. Interaction of Hsp with such receptors may have at least two important consequences:

cytokine secretion by the dendritic cell that promotes cellular immunity and internalization of the Hsp and bound polypeptides by the dendritic cell into the class I pathway of antigen presentation.

### *Scientific Foundation of Stressgen Technology*

Dendritic cells express receptors that specifically recognize Hsp. As a result, they can capture and process Hsp fusions, which are Hsp covalently linked to antigens. The Hsp fusions then induce cellular immune responses to the antigen present in the fusions, such as a viral protein. Preclinical data from both in vitro and in vivo models demonstrate that Hsp fusions trigger innate immune responses; the cells from the innate response signal the adaptive immune system to use its protection mechanisms. We seek to develop a new class of therapeutic products based on this ability of Hsp fusions to induce antigen-specific CTL responses.

We call Hsp fusions "immunotherapeutics" based on their ability to stimulate the body's own immune system to attack a pathogen, as does a vaccine. Unlike existing preventative vaccines, Hsp fusions trigger the immune system to respond to infected cells and cancers already present in the body. Since preclinical research has shown that Hsp fusions induce CD8+ CTL responses in CD4+-deficient animals, it is possible that even immunosuppressed individuals such as HIV+ patients and transplant recipients may be treated effectively with our platform technology.

Potentially, Hsp fusions can be created with any number of disease-specific protein antigens. Our most developed product, HspE7, is a recombinant fusion protein composed of the HPV protein E7 and a bacterial Hsp. In all types of HPV infection, whether "low risk," including warts or "high risk," including pre-cancer and cancer, the E7 protein theoretically provides a precise target by which the immune system can recognize and attack HPV-infected cells. Induction of E7-specific cellular immunity by Hsp fusions offers a new approach to the immunotherapy of HPV-associated diseases.

In pre-clinical studies conducted using an animal model, administration of HspE7 has been shown to prevent the growth of, and cause the destruction of, tumors that express the HPV E7 protein. Only the fusion protein induces significant tumor regression and long-term survival in these studies. Neither the E7 antigen nor the Hsp alone, nor a mixture of the two, is effective. The requirement for a covalent attachment between the Hsp and the E7 protein may be explained by the presence of Hsp receptors on dendritic cells. By virtue of its covalent attachment to the Hsp, the E7 protein is targeted to the dendritic cell, internalized and presented as E7 peptides by the class I pathway to activate killer T cells. These E7-specific killer T cells may then be able to survey for and destroy E7 containing cancer cells.

Clinical observations made in phase II trials for AIN and genital warts indicate that treatment with HspE7 leads to disease improvement or clearance that is not restricted to lesions containing a specific type of HPV. These original and surprising findings demonstrate the potential for HspE7 to treat diseases caused by multiple HPV types. Although the E7 protein present in HspE7 was derived from HPV type 16, which is known to be associated with about half of all cervical cancers and about 20% of pre-cancerous lesions known as anogenital dysplasias, our clinical data strongly suggests that HspE7 can induce cross-reactive T cell responses in genital warts and RRP, which primarily are caused by HPV types 6 and 11.

### *Human Papillomavirus Indications*

HPV indications can be easily recognizable, like genital warts, or latent. Infected individuals with no visible symptoms may not be aware that they have a persistent viral infection, increasing their risk of developing complications and of transmitting the virus to others. HPV is highly contagious and can be spread even when condoms are used. Fifty to 75% of sexually active men and women acquire genital HPV infection at some point in their lives.

Although there are over 100 different types of HPV, most research focuses on the approximately one-third infecting genital epithelial tissue and primarily spread through sexual contact. Researchers differentiate among the HPV types using letter and number designations. The E7 protein from high-risk HPV types (associated with a high risk of cancer) is involved in the malignant transformation of infected epithelial cells. These HPV types cause premalignant and cancerous cervical and anal conditions, including high-grade and low-grade dysplasias and cancer. Low-risk types of HPV typically cause internal and external genital warts.

### *Genital Warts*

Approximately two-thirds of people who have sexual contact with a partner with genital warts develop warts themselves, usually within three months of contact, according to the U.S. National Institute of Allergy and Infectious Diseases (the NIAID). The incidence of genital warts is an estimated 1 million new cases in the U.S. each year, according to a July 1999 NIAID Fact Sheet. Of those patients, an estimated 67% are women. Although the lesions may spontaneously regress, recurrence is typical. The lesions also frequently reappear after treatment.

### *Recurrent Respiratory Papillomatosis*

Recurrent Respiratory Papillomatosis is caused by the same types of papillomavirus that cause genital warts. In fact, the term papilloma means wart. Rather than infecting genital tissue, the papillomas in RRP occur primarily on the vocal cords of children born to mothers infected with HPV. The papillomas can spread into the trachea and lungs. Over 2,000 new cases of pediatric RRP and over 3,500 new cases of adult RRP are diagnosed annually in the U.S., according to a study published in 1995 based upon a survey of members of the American Society of Pediatric Otolaryngology, members of the American Bronchoesophagological Association and certified U.S. otolaryngologists. Patients with RRP can die from airway obstruction, cancerous transformation, overwhelming spread of the disease, growth of papillomas in the lungs or complications of surgical treatments. There are no drugs or immunotherapies approved for RRP in the U.S. Pediatric patients tend to have about 5 surgeries per year and some children have hundreds of procedures during their lifetime.

### *Cervical Intraepithelial Neoplasia and Cervical Cancer*

Cervical Intraepithelial Neoplasia, also known as cervical dysplasia, is characterized by the presence in the cervix of abnormal cells that often precede cervical cancer. The abnormal cells are associated with the malignant transformation of epithelial cells infected with HPV virus. Such cells can be detected through regular Pap smear screening. In the U.S. more than 1.2

million women a year are diagnosed with low-grade cervical dysplasia, according to National Cancer Institute estimates. Another 200,000 to 300,000 are diagnosed with high-grade cervical dysplasia in the U.S. each year, according to a December 1999 report of the Centers for Disease Control. Worldwide, the problem is much larger. The current treatment for CIN, which involves local surgical techniques, is not always effective. Surgical treatment may not remove all dysplastic cells and does not treat the underlying viral infection. In addition, surgery can result in complications such as reduced fertility.

CIN often precedes cervical cancer, a worldwide public health problem particularly in countries where routine Pap smears are not practiced. American Cancer Society estimates for 2002 predicted that approximately 13,000 women in the U.S. would be diagnosed with invasive cervical cancer and that about 4,100 patients would die from the disease. Globally there are approximately 500,000 new cases of cervical cancer identified each year, resulting in nearly 300,000 deaths. Cervical cancer is the second most important cancer in women after breast cancer, according to a World Health Organization February 1999 press release. Although death rates from cervical cancer have been decreasing, invasive cervical cancer continues to be associated with extreme morbidity.

#### *Anal Intraepithelial Neoplasia*

Anal Intraepithelial Neoplasia is characterized by the presence of abnormal cells that may precede anal cancer. Data extrapolated from studies of homosexual and bisexual men and the anal cancer population suggests that there may be 500,000 new cases per year in the U.S. Patients are not commonly screened for AIN; however, there is increasing awareness of the condition. No standard therapies exist for AIN.

#### ***Indications Targeted in Early Stage Development and Research Programs***

All of the indications described above are associated with HPV, so are candidates for treatment with HspE7. We are also using our platform technology to create fusions of heat shock proteins with antigens from other sources. We are testing CoVal™ fusions of heat shock proteins with antigens from hepatitis B and herpes simplex to determine whether to advance treatments for those indications into pre-clinical testing and clinical trials. We consider hepatitis C another logical target for a CoVal™ fusion.

#### *Hepatitis B*

Chronic hepatitis B is a disease of the liver caused by the hepatitis B virus. Infection with HBV is characterized by jaundice, fatigue, abdominal pain and other symptoms, with many patients developing liver cirrhosis and cancer. Although safe and effective preventative vaccines exist, there are estimated to be 1,000,000 to 1,250,000 cases of chronic hepatitis B in the U.S., according to the Centers for Disease Control and Prevention. In addition, there are between 140,000 and 320,000 new cases of hepatitis B in the U.S. each year, resulting in 4,000 to 5,000 deaths according to the American Social Health Association. Worldwide, about 1,000,000 deaths are attributable to HBV infection and its complications annually, according to the World Health Organization. Due to the large infected population and small percentage of the public

being vaccinated for the disease, the need for new and effective therapies for chronic hepatitis B virus infection remains great.

### *Hepatitis C*

Hepatitis C causes symptoms similar to those of hepatitis B, but is caused by the hepatitis C virus. Chronic hepatitis C can cause cirrhosis, liver failure, and liver cancer. HCV is spread through contact with blood and other bodily fluids. Currently, there are six known hepatitis C genotypes, and more than 50 subtypes. The relative prevalence of different genotypes differs by geographic region. It is estimated that 3.9 million people in the U.S. (1.8% of the population) have been infected with HCV and that 2.7 million are chronically infected. Worldwide there is an estimated 200 million cases. In the U.S. 8,000 to 10,000 deaths each year are currently attributed to HCV. Although about 80% of patients are currently asymptomatic, researchers predict that over the next 10 to 20 years chronic hepatitis C will become a major burden on the health care system as patients progress to end-stage liver disease. The efficacy of current treatments varies depending upon the genotype of the virus, but no currently available therapy can eradicate the virus or do more than delay the progression of the disease. No vaccine is available.

### *Herpes Simplex Virus*

Herpes Simplex Virus causes genital herpes. The prevalence of herpes simplex type-2 (HSV-2) has increased by 30% since the late 1970s and is now detectable in about one in five persons 12 years of age or older in the US, according to the NIAID. An estimated 45 million Americans are already infected with genital herpes, and there are an additional 500,000 to 1,000,000 new cases each year, the NIAID has written. Since HSV remains dormant in infected persons for their lifetime, genital herpes is a recurrent disease, consisting of alternating episodes of virus reactivation with virus shedding, followed by resolution of the outbreak and return to virus dormancy. Some episodes of reactivation are associated with skin blistering in the genital region, causing physical and psychological discomfort. Because most episodes of the infection are asymptomatic, people having an outbreak may not be aware that they are transmitting herpes. As a result, HSV-2 is expected to continue to spread rapidly. Except in newborns, genital herpes is not life-threatening. Nonetheless, it is distressing and can contribute to the spread of other sexually transmitted diseases.

### **HspE7 Development Program**

We are dedicating most of our resources to commercializing HspE7 as quickly as we can. The focus of our HspE7 development program has evolved over time to take advantage of the results from clinical trials, to ensure we are addressing the broadest potential market for the product, and to capitalize upon the resources of third-parties interested in using HspE7 to treat specific indications.

We originally designed HspE7 to be a non-surgical approach for reducing the risk of progression of CIN to cervical cancer. Because surgical treatments exist for CIN and cervical cancer, we realized that it might be easier and faster to obtain regulatory approval for other HPV indications.

We began focusing on AIN, which leads to anal cancer, based on the advice of scientific advisors, the similarities of those conditions to CIN and cervical cancer, the clear unmet medical needs for the conditions and the lack of widely accepted standard treatments for AIN. The U.S. National Cancer Institute has recognized the potential of HspE7 to prevent cancers caused by HPV. As a result, in 1999 its Division of Cancer Treatment and Diagnosis signed a Clinical Trials Agreement with us to sponsor clinical trials using HspE7.

Our cancer-related research indirectly led us to explore HspE7 for the treatment of genital warts. In the course of an AIN clinical trial, we discovered that genital warts regressed in patients with both AIN and genital warts. The size of the genital warts market made it more attractive commercially than AIN or CIN. To further accelerate the time to market, we sought orphan drug status for RRP, a life-threatening condition in which the warts occur in the upper airways. As we had hoped, the U.S. Food and Drug Administration granted orphan drug status for HspE7 for the treatment of RRP. We continued to accrue clinical trials data regarding AIN and genital warts while we began an RRP trial.

Our AIN and genital warts data drew the interest of potential collaborators. In June 2002 we signed a second agreement with the U.S. National Cancer Institute, in this case with the Division of Cancer Prevention, to sponsor additional clinical trials. In the same month, we signed a collaboration agreement with Roche for the development of HspE7, which we restated in December 2003. In December 2003, the U.S. Food and Drug Administration also designated HspE7 as a Fast Track Product development program for the treatment of patients suffering from RRP.

We have recently completed an open-label RRP trial in pediatric patients requiring frequent surgery and an AIN trial; we are analyzing the results. The AIDS Malignancy Consortium of the National Cancer Institute is evaluating HspE7 in HIV-positive patients with high-grade anal dysplasia. Several other trials with HspE7 are planned. Based on our findings from the clinical trials we have run to date, advice from an ad hoc clinical advisory board, market research, and our experience with the regulatory approval process, we are targeting RRP as the first market for HspE7. We hope to expand the indications for HspE7 to some or all of genital warts, AIN, anal cancer, CIN, and cervical cancer after the product is approved for RRP.

#### ***Data from HspE7 Clinical Trials***

Most of our clinical trials have been conducted in the U.S. using a 500 ug dose of HspE7 given once a month for a total of three doses over 60 days. We have released findings based on data from clinical trials including:

- An interim review of data from our open-label pediatric RRP trial in 27 patients
- a 6 month low dose, double-blind placebo controlled trial of AIN patients, most of whom then rolled-over to a 6 month 3x500 ug dose open label arm

- an open registry of AIN patients, to follow up from a completed low dose, double-blind, placebo controlled trial and a completed 3x500 ug dose open-label trial, for a total of 24 months
- a chart review of patient from the registry or its predecessor trials, following for a total of 24 months a subset of AIN patients who also had genital warts

The results suggest that the 3x500 ug dose of HspE7 is active against multiple types of HPV. Data from these studies showed that:

- treatment with HspE7 increased the time interval between required RRP surgeries and reduced the frequency of surgery in these patients with moderate and severe RRP;
- 44% of AIN patients achieved complete resolution of high grade anal dysplasia, a precursor to anal cancer, by 15 months
- 95% of AIN patients showed pathological downgrade from high grade anal dysplasia to low grade dysplasia or no dysplasia by 15 months, indicating that HspE7 could potentially eliminate the need for surgery
- 80% of AIN patients who also had genital warts achieved complete remission of genital warts at 24 months, indicating broad-spectrum efficacy of HspE7

Results from a double blind placebo controlled phase II trial in measurable external warts showed that, at six months:

- Genital warts decreased in size by a median of 53% compared to a median of 16% in patients treated with placebo
- The complete response rate for patients with genital warts varied depending on the gender of the patient and location of the warts. Women had a 62% complete response rate, compared to 20% of female patients treated with placebo. Men with anal and perianal genital warts achieved a 42% complete response rate, compared to 25% of such patients treated with placebo. As with alternative treatments, penile warts responded less well than patients with warts in other locations.

Observations of complete response in genital warts patients during the time period 12 to 24 months from treatment, and of few or no recurrences to date, contrasts with the data for treatment of warts with surgery or topical therapy in which rapid recurrence is common.

Safety data for treatment with HspE7 continue to be accumulated. The predominant adverse experience noted from HspE7 treatment at various doses and schedules is injection site reaction, mild to moderate in severity, clearing in hours to days without treatment. Mild to moderate flu-like symptoms are also observed in some patients.

## **Status of Early Stage Research Programs**

We are using our proprietary technology of fusing heat shock proteins to antigens to create Hsp fusions with antigens other than E7. Our most active early stage programs involve therapies for chronic hepatitis B infection and herpes simplex virus. We are compiling preclinical data to support an Investigational New Drug filing for a fusion of an Hsp and a selected HBV antigen. In mice our HBV fusions have been shown to elicit cytotoxic T lymphocytes (CTL) that recognize the HBV antigen, suggesting such T cells would be capable of killing HBV-infected cells. The T cells have also shown to produce the cytokine interferon gamma, which is known to have anti-viral activity. The results of these preclinical studies demonstrate the potential efficacy of Hsp-HBV antigen fusions in the immunotherapy of chronic HBV infection. We believe that our HBV program could offer hope in countering the disease's significant worldwide impact on human health.

We are assessing the development of Hsp fusion proteins for the immunotherapy of genital herpes. Presently, we are including a number of HSV-2 proteins in Hsp fusions and testing them in animal models for induction of immune responses to the HSV antigens. An immunotherapy that can induce cellular immunity specific for HSV-2 antigens may lead to a treatment for genital herpes to reduce the number or duration of reactivation episodes or prevent them entirely.

## **Intellectual Property**

Our intellectual property protection policy is to file and prosecute patent applications relevant to the inventions that we consider meaningful to our business. We also rely upon unpatented trade secrets, know-how and continuing technological innovation to develop and maintain a competitive position. We devote substantial management attention and resources to maintaining patents and licenses and conducting an assertive patent prosecution strategy.

We have a worldwide, exclusive license agreement with the Whitehead Institute for our core fusion technology, giving us rights to various patents, pending applications, continuation-in-part applications and their foreign counterparts. Pursuant to the license agreement we fund the prosecution of the patent applications, which currently include applications in the U.S., Canada, Europe and Japan. Two U.S. patents, which will expire in 2019, and a European patent, which will expire in 2014, have been granted based on these Whitehead applications. We are vigorously defending challenges to these patents, which cover Hsp fusions with viral or cancer-associated antigens and their use as immunotherapeutics. Independently, we have filed additional patent applications directed to Hsp fusions with other viral antigens, including HPV E6 and E7, and their use as immunotherapeutics. U.S. and European patents based on these applications were granted in 2003. We also hold issued U.S. patents related to the detection of elevated levels of Hsp expression. Some of the U.S. patent applications received pre-GATT filing status, meaning that their terms extend for 17 years after the date of grant, rather than 20 years from the earliest date of filing.

Interpretation and evaluation of biopharmaceutical or biotechnology patent claims present complex and often novel legal and factual questions. We cannot be sure that our pending applications will result in issued patents, that the issued patents will be held valid and

enforceable if challenged, or that a competitor will not be able to circumvent an issued patent by the development or adoption of a competitive non-infringing product or process.

### **Research and Development Collaborations**

We have two clinical trials agreements with the U.S. National Cancer Institute for the co-development of our lead product, HspE7, in the treatment of cancer. The NCI is the U.S. government's principal institute for cancer research and training. The clinical trials agreements allow the NCI to develop a general plan for clinical development of HspE7 for cancer-related indications, solicit clinical research protocols from independent investigators and cooperative research groups, and sponsor and fund their studies. We are expected to provide clinical grade HspE7 for the investigators to use in their studies but do not provide funding. The first clinical trial sponsored by the NCI, testing HspE7 in HIV-positive patients with high-grade anal dysplasia, began in December 2002. The collaboration with the NCI enables studies of HspE7 for the treatment of dysplasias and cancer to progress, while we focus on RRP.

A third-party investigator from a university is running a phase I/II trial of HspE7 in cervical dysplasia under the investigator's investigational new drug application. As with the NCI trials, we have access to data from the trial in return for providing HspE7.

We have a number of collaborative or sponsored research agreements that we believe provide us with important sources of research data and could lead to technology development opportunities. We have entered into an agreement with the National Institute of Allergy and Infectious Diseases to test our hepatitis B candidate in preclinical models. We are also sponsoring academic institutions to evaluate our hepatitis B candidate in animal models and to perform herpes simplex research with our CoVal<sup>TM</sup> fusions.

### **Manufacturing**

We are currently working with an independent contractor to develop a quality controlled and quality assured process for producing HspE7, based on a set of standard operating procedures, analytical methods and specifications that will allow HspE7 to be manufactured in commercial quantities in accordance with current good manufacturing practice and other regulations. We expect that our dependence on third-parties for the process development and manufacture of heat shock protein fusions will continue for the foreseeable future.

### **Bioreagent Business**

Our bioreagent business supplies biomedical research reagents to researchers in not-for-profit research organizations and commercial institutions worldwide. The primary products of the business involve antibodies, proteins, DNA products, ELISA kits, lysates and extracts, for use in studying cellular stress response pathways, including oxidative stress, apoptosis, neurobiology and more. Although we contract with third-party distributors in thirty-five countries, our primary markets are in North America, Europe and Asia. Sales have been approximately 65% from the U.S., 5% from Canada, 20% from Europe and 10% from the rest of the world, in each of the last three years. We do not believe that any single customer is material to our bioreagent

business. Demand for our products tends to increase slightly when academic institutions in the Northern Hemisphere are in session.

We manufacture products for inventory and ship products shortly after the receipt of orders, and anticipate that we will continue to do so in the future. Accordingly, we currently do not have a significant backlog and do not anticipate that we will develop a material backlog in the future. We believe the quantity of inventory we maintain is adequate to ensure reasonable customer service while limiting the volatility of inventory levels. Inventory quantities can fluctuate significantly as we balance varying customer demand against fluctuating supplies of reagents available to us. We buy materials for our products from many suppliers, and we are not dependent on any one supplier or group of suppliers. Raw materials are generally readily available at competitive prices from a number of suppliers. We believe that we will be able to continue to acquire and produce our products in quantities sufficient to meet our customers' current requirements.

We require patent licenses to sell many of our products. However, because our sales are spread over more than 400 products, we believe that no individual patent or license is material to our bioreagent business. In each of the last three years, three product groups have contributed more than 15% of the revenue of the bioreagent business: monoclonal antibodies have contributed approximately 30% of revenue; polyclonal antibodies have contributed approximately 35% of revenue and proteins have contributed approximately 20% of revenue.

### **Government Regulation and Product Approval Process**

In the U.S. the Food and Drug Administration (FDA) regulates drugs and biological products. In Canada the *Food and Drug Act* (Canada), and the rules and regulations promulgated thereunder, govern the production and manufacturing of our products and our research and development activities; the Health Products and Food Branch (HPFB) Inspectorate enforces these rules and regulations. In these and other jurisdictions, applicable drug licensing laws require carefully controlled research and testing of products, governmental review and approval of results prior to marketing therapeutic products, licensure of manufacturing facilities and adherence to good manufacturing practices during production.

The principal activities which must be completed before obtaining approval for marketing in the U.S. and Canada are the completion of (1) development of a well-controlled process of manufacturing, (2) preclinical studies of safety and pharmacology, and (3) studies of safety and efficacy in humans. Pre-clinical studies are conducted to test chemistry, pharmacology and efficacy. Successful pre-clinical results, which entail achieving potentially valuable pharmacological activity combined with an acceptably low level of toxicity, enable the manufacturer of the new drug to file an investigational new drug application to begin clinical trials involving humans. An investigational new drug application must be filed with and accepted by the FDA or HPFB, as applicable, before human clinical trials may begin.

Phase I clinical trials consist of testing a product in a small number of humans for its safety (toxicity), dose tolerance and pharmacokinetic properties including absorption, distribution, metabolism and elimination. Phase II clinical trials usually involve a larger patient population than is required for phase I trials and are conducted to evaluate the effectiveness of a product in

patients having the disease or medical condition for which the product is indicated. These trials also serve to identify possible common short-term side effects and risks in a larger group of patients. Potential dosing regimens may also be evaluated during phase II trials. Phase III clinical trials involve conducting tests in an expanded patient population at geographically dispersed sites to establish clinical safety and effectiveness. These trials usually involve comparison to a standard treatment or to no treatment. These trials also generate information from which the overall benefit-risk relationship relating to the drug can be determined and provide a basis for drug labeling.

Two key factors influencing the rate of progression of clinical trials are the rate at which patients can be accrued to participate in the research program and whether effective treatments are currently available for the disease the drug is intended to treat. Patient accrual can depend upon the incidence and severity of the disease and the alternative treatments available.

Upon completion of all clinical studies, the results of these studies are submitted to the U.S. FDA as part of a biologics license application, in the case of a biological product, or to Canada's HPFB as part of a new drug submission, to obtain approval to commence marketing the product. An establishment license application to produce a product must also be submitted for approval by the FDA or HPFB. Additional requirements would apply for an application to market a human prophylactic vaccine.

After a marketing approval is obtained, further studies, including post-market studies, may be required to provide additional data on safety and efficacy necessary to gain approval for the use of a product as a treatment for clinical indications other than those for which the product was initially tested. Also, the FDA or HPFB may require post-market surveillance programs to monitor a product's side effects.

As well as receiving pre-licensing approval, manufacturing facilities must conform on an ongoing basis with Good Manufacturing Practices, or GMP. After the establishment is licensed for the manufacture of any product, manufacturers are subject to periodic inspections by regulatory authorities.

Whether or not FDA or HPFB approval has been obtained, approval of a product by comparable regulatory authorities in Europe and other countries will be necessary prior to commencement of marketing the product in such countries. Each country may impose their own requirements and may refuse to grant, or may require additional data before granting, an approval even though the relevant product has been approved by another authority.

We are also subject to various federal, state, local and international laws, regulations and recommendations relating to safe working conditions, laboratory manufacturing practices and the use and disposal of hazardous or potentially hazardous substances, including radioactive compounds and infectious disease agents, used in connection with our research work.

### **Competition**

We are subject to competition from products that use different approaches or means of accomplishing a similar therapeutic effect as our CoVal<sup>TM</sup> fusion products. Many pharmaceutical and biotechnology companies also focus their research and product development

programs on the treatment of the same therapeutic indications as ours, including HPV, hepatitis B virus, hepatitis C virus, herpes simplex virus and cancer.

Potential competitors that are developing products to treat HPV indications use approaches including therapeutic vaccines, immunotherapies, immunomodulators, topical therapies and small molecule drugs. For example, Transgene S.A., Zycos Inc. and Xenova Group plc are conducting clinical trials with different formulations of HPV antigens as therapeutic vaccines and immunotherapies.

Other potential competitors are performing research and developing therapeutic products based on the intrinsic nature of stress proteins to assist the body in fighting infection and related cancers. While our technology focuses on heat shock proteins covalently fused to antigens, there are other ways to potentially use heat shock proteins to modulate immune responses. Companies including Antigenics Inc. and Mojave Therapeutics, Inc. are using stress protein-related approaches to stimulate or modulate the body's immune system in therapeutic applications. Other companies such as Conforma Therapeutics and Vernalis plc are developing small molecule drugs to modulate heat shock protein expression in cells as another approach for cancer therapy.

Competition in our industry may increase over time due to rapid and substantial changes in technology, and other critical inputs required for product development and commercialization. Many of our competitors have greater human and financial resources dedicated to product development and human clinical testing than we do, as well as substantial marketing and financial resources. Acquisitions of, or investments in, competing pharmaceutical and biotechnology companies by other firms could increase such competitors' financial, marketing and other resources. Technological developments could render our proposed products or technologies non-competitive.

The diseases we are targeting are currently managed through a variety of therapeutic and surgical approaches. For example, genital warts can be treated by topical creams and ointments, cryosurgery, freezing, electro-cauterization and laser treatment. Some papillomas and cancers caused by HPV can be treated surgically.

In the stress protein bioreagent market current direct competition is limited. A few companies have a broad line of competing products, such as Affinity Bioreagents Inc.; several larger companies have introduced a limited range of similar products as ours. Many of our product licenses are non-exclusive, so competition from other suppliers could increase in the future.

## **Human Resources**

As of January 31, 2004 we employed approximately 95 personnel, of which over 50 were engaged in, directly or indirectly, research and development efforts. Of the scientific persons employed, two hold an M.D., twelve hold Ph.D.s, and the balance hold either M.Sc. or B.Sc. degrees or other diplomas. Our employees are not covered by any collective bargaining agreement. All employees are required to execute confidentiality and assignment of invention agreements as a condition of their employment.

## **Availability of Information**

Our annual report on Form 10-K and quarterly reports on Form 10-Q are available on our website, [www.stressgen.com](http://www.stressgen.com), free of charge, as soon as reasonably practicable after such material is filed with the U.S. and Canadian securities regulatory authorities. Our website also provides links for users to find our filings on the websites maintained by the U.S. and Canadian securities regulatory authorities. We consider those sites to be the appropriate sources for reports that are filed with the securities regulatory authorities of only the U.S. or only Canada, rather than with both countries. Paper copies of our most recent filings are available from our Investor Relations department free of charge upon request.

## **FACTORS THAT MAY AFFECT FUTURE PERFORMANCE**

**Before investing in our common stock you should carefully consider the following risk factors, the other information included herein and the information included in our other reports and filings. Our business, financial condition, and the trading price of our common stock could be adversely affected by these and other risks.**

### **We are an Early Stage Development Company**

Our biotechnology business is still at an early stage of development. Significant additional research and development and clinical trials must be completed before our technology can be commercialized. We have not completed the development of any therapeutic products and, therefore, have not begun to market or generate revenues from the commercialization of any therapeutic products. We have undertaken only limited human clinical trials for HspE7 and cannot assure you that subsequent trials will generate comparable results, that the results obtained from laboratory or research studies for our other products will be replicated in human studies, that our human studies will demonstrate efficacy or that our studies and trials will not identify undesirable side effects of our products. There are no assurances that any of our therapeutic products will:

- meet applicable health regulatory standards
- obtain required regulatory approvals or clearances
- be produced in commercial quantities at reasonable costs
- be successfully marketed or
- be profitable enough that we will recoup the investment made in such product candidates.

None of our therapeutic product candidates are expected to be commercially available for several years. It is possible that we will not successfully develop any therapeutic products.

### **We Have a History of Operating Losses and May Never Become Profitable**

We have not recorded any revenues from the sale of therapeutic products and have accumulated

substantial net losses. We expect we will incur continued losses for at least the next several years while our primary activities are research, development, and clinical trials. To become profitable we, either alone or with one or more partners, must develop, manufacture and successfully market therapeutic product candidates.

### **We Must Obtain Additional Financing to Execute Our Business Plan**

The revenues from the production and sale of bioreagents and the projected revenues from collaborators are not adequate to support either the development of HspE7 under the restructured Roche Collaboration Agreement or our other therapeutic product development programs. We will need substantial additional funds to pursue further research and development; carry out clinical trials; obtain regulatory approvals; file, prosecute, defend and enforce our intellectual property rights and market our products. We will seek additional funds through public or private equity or debt financing, strategic transactions and/or from other sources. We could enter into collaborative arrangements for the development of particular products that would lead to our relinquishing some or all rights to the related technology or products.

There are no assurances that future funding will be available on favorable terms or at all. If additional funding is not obtained, we will need to reduce, defer or cancel development programs, planned initiatives or overhead expenditures, to the extent necessary. The failure to fund our capital requirements would have a material adverse effect on our business, financial condition and results of operations.

### **Our Success Depends On Collaborative Partners, Licensees and Other Third Parties Over Whom We Have Limited Control**

Due to the complexity of the process of developing therapeutics, our core business depends on arrangements with pharmaceutical companies, corporate and academic collaborators, licensors, licensees and others for the research, development, clinical testing, technology rights, manufacturing, marketing and commercialization of our products. We have various research collaborations and outsource many other business functions, including clinical trials and manufacturing. Our license agreements could obligate us to diligently bring potential products to market, make milestone payments and royalties that, in some instances, could be substantial, and incur the costs of filing and prosecuting patent applications. There are no assurances that we will be able to establish or maintain collaborations that are important to our business on favorable terms, or at all.

A number of risks arise from our dependence on collaborative agreements with third parties. Product development and commercialization efforts could be adversely affected if any collaborative partner:

- terminates or suspends its agreement with us
- causes delays
- fails to timely develop or manufacture in adequate quantities a substance needed in order to conduct clinical trials

- fails to adequately perform clinical trials
- determines not to develop, manufacture or commercialize a product to which it has rights or
- otherwise fails to meet its contractual obligations.

Our collaborative partners could pursue other technologies or develop alternative products that could compete with the products we are developing.

**The Profitability of Our Products Will Depend in Part on Our Ability to Protect Proprietary Rights and Operate Without Infringing the Proprietary Rights of Others**

The profitability of our products will depend in part on our ability to obtain and maintain patents and licenses and preserve trade secrets, and the period our intellectual property remains exclusive. We must also operate without infringing the proprietary rights of third parties and without third parties circumventing our rights. The patent positions of pharmaceutical and biotechnology enterprises, including ours, are uncertain and involve complex legal and factual questions for which important legal principles are largely unresolved. For example, no consistent policy has emerged regarding the breadth of biotechnology patent claims that are granted by the U.S. Patent and Trademark Office or enforced by the U.S. federal courts. In addition, the scope of the originally claimed subject matter in a patent application can be significantly reduced before a patent is issued. The biotechnology patent situation outside the U.S. is even more uncertain, is currently undergoing review and revision in many countries, and may not protect our intellectual property rights to the same extent as the laws of the U.S. Because patent applications are maintained in secrecy in some cases, we cannot be certain that we or our licensors are the first creators of inventions described in our pending patent applications or patents or the first to file patent applications for such inventions.

Other companies may independently develop similar products and design around any patented products we develop. We cannot assure you that:

- any of our patent applications will result in the issuance of patents
- we will develop additional patentable products
- the patents we have been issued will provide us with any competitive advantages
- the patents of others will not impede our ability to do business or
- third parties will not be able to circumvent our patents.

On October 22, 2002 Antigenics Inc. announced that it had filed an opposition in the European Patent Office to a European patent and requests for re-examination in the U.S. Patent and Trademark Office of two U.S. patents we licensed in connection with our platform technology. In October 2003 Antigenics filed an opposition in the European Patent Office to an additional, product specific, European patent. It could take several years to obtain results from these proceedings. Until we receive final results from the opposition and re-examination processes,

we will not be able to assure investors of the success of our planned vigorous defense of the patents.

A number of pharmaceutical, biotechnology, research and academic companies and institutions have developed technologies, filed patent applications or received patents on technologies that may relate to our business. If these technologies, applications or patents conflict with ours, the scope of our current or future patents could be limited or our patent applications could be denied. Our business may be adversely affected if competitors independently develop competing technologies, especially if we do not obtain, or obtain only narrow, patent protection. If patents that cover our activities are issued to other companies, we may not be able to obtain licenses at a reasonable cost, or at all; develop our technology; or introduce, manufacture or sell the products we have planned.

Patent litigation is becoming widespread in the biotechnology industry. Such litigation may affect our efforts to form collaborations, to conduct research or development, to conduct clinical testing or to manufacture or market any products under development. There are no assurances that our patents would be held valid or enforceable by a court or that a competitor's technology or product would be found to infringe our patents in the event of patent litigation. Our business could be materially affected by an adverse outcome to such litigation. Similarly, we may need to participate in interference proceedings declared by the U.S. Patent and Trademark Office or equivalent international authorities to determine priority of invention. We could incur substantial costs and devote significant management resources to defend our patent position or to seek a declaration that another company's patents are invalid.

Much of our know-how and technology may not be patentable, though it may constitute trade secrets. There are no assurances that we will be able to meaningfully protect our trade secrets. We cannot assure you that any of our existing confidentiality agreements with employees, consultants, advisors or collaborators will provide meaningful protection for our trade secrets, know-how or other proprietary information in the event of any unauthorized use or disclosure. Collaborators, advisors or consultants may dispute the ownership of proprietary rights to our technology, for example by asserting that they developed the technology independently.

### **We May Encounter Difficulties in Manufacturing our Products**

Our manufacturing experience in bioreagents is not directly applicable to the manufacture of therapeutic products. We have not yet introduced any therapeutic products and have no experience manufacturing immunotherapeutics ourselves. Before our products can be profitable, they must be produced in commercial quantities in a cost-effective manufacturing process that complies with regulatory requirements, including GMP, production and quality control regulations. Because we do not have facilities for the production of therapeutic products such as HspE7, we contract with third parties for process development, the scale-up of manufacturing our products from the laboratory bench to commercial quantities, manufacturing of bulk materials, product characterization, filling the product into vials, packaging and related processes. If we cannot arrange for or maintain commercial-scale manufacturing on acceptable terms, or if there are delays or difficulties in transitioning our products between the contractors performing different aspects of the manufacturing process, we may not be able to conduct clinical trials, obtain regulatory approval or meet demand for our products.

Production of our products could require raw materials which are scarce or which can be obtained only from a limited number of sources. If our manufacturers were unable to obtain adequate supplies of such raw materials, the development, regulatory approval and marketing of our products could be delayed.

### **We Could Need More Clinical Trials or Take More Time to Complete Our Clinical Trials Than We Have Planned**

Clinical trials vary in design by factors including dosage, end points, length, controls, and numbers and types of patients enrolled. We may need to conduct a series of trials to demonstrate the safety and efficacy of our products. The results of these trials may not demonstrate safety or efficacy sufficiently for regulatory authorities to approve our products.

Regulatory authorities may require us to determine whether our products delay or prevent disease recurrence. Clinical trials to show that a disease does not recur take longer to complete than clinical trials that end when patients stop having specific symptoms. The actual schedules for our clinical trials could vary dramatically from the forecasted schedules due to factors including changes in trial design, conflicts with the schedules of participating clinicians and clinical institutions, delayed patient accrual and changes affecting product supplies for clinical trials.

We rely on collaborators, including academic institutions, governmental agencies and clinical research organizations, to conduct, supervise, monitor and design some or all aspects of clinical trials involving our products. The National Cancer Institute is sponsoring some HspE7 clinical trials. Since these trials depend on governmental participation and funding, we have less control over their timing and design than trials we sponsor. Delays in or failure to commence or complete any planned clinical trials could delay the ultimate timelines for product release. Such delays could reduce investors' confidence in our ability to develop products, likely causing our share price to decrease.

### **We May Not Be Able to Obtain the Regulatory Approvals or Clearances That Are Necessary to Commercialize Our Products**

The U.S., Canada and other countries impose significant statutory and regulatory obligations upon the manufacture and sale of human therapeutic products. Each regulatory authority typically has a lengthy approval process in which it examines pre-clinical and clinical data and the facilities in which the product is manufactured. Regulatory submissions must meet complex criteria to demonstrate the safety and efficacy of the ultimate products. Addressing these criteria requires considerable data collection, verification and analysis. We may spend time and money preparing regulatory submissions or applications without assurances as to whether they will be approved on a timely basis or at all.

Our product candidates, some of which are currently in the early stages of development, will require significant additional development and pre-clinical and clinical testing prior to their commercialization. These steps and the process of obtaining required approvals and clearances can be costly and time-consuming. If our potential products are not successfully developed, cannot be proven to be safe and effective through clinical trials, or do not receive applicable

regulatory approvals and clearances, or if there are delays in the process:

- the commercialization of our products could be adversely affected;
- any competitive advantages of the products could be diminished; and
- revenues or collaborative milestones from the products could be reduced or delayed.

Governmental and regulatory authorities may approve a product candidate for fewer indications or narrower circumstances than requested or may condition approval on the performance of post-marketing studies for a product candidate. Even if a product receives regulatory approval and clearance, it may later exhibit adverse side effects that limit or prevent its widespread use or that force us to withdraw the product from the market.

Any marketed product and its manufacturer will continue to be subject to strict regulation after approval. Results of post-marketing programs may limit or expand the further marketing of products. Unforeseen problems with an approved product or any violation of regulations could result in restrictions on the product, including its withdrawal from the market and possible civil actions.

The manufacturers of our products will be required to comply with applicable good manufacturing practices regulations, which include requirements relating to quality control and quality assurance, as well as the maintenance of records and documentation. If the manufacturers cannot comply with regulatory requirements, including applicable good manufacturing practice requirements, we may not be allowed to develop or market the product candidates. If we or our manufacturers fail to comply with applicable regulatory requirements at any stage during the regulatory process, we may be subject to sanctions, including fines, product recalls or seizures, injunctions, refusal of regulatory agencies to review pending market approval applications or supplements to approve applications, total or partial suspension of production, civil penalties, withdrawals of previously approved marketing applications and criminal prosecution.

### **Competitors May Develop and Market Drugs That Are Less Expensive, More Effective or Safer, Making Our Products Obsolete or Uncompetitive**

Many competitors and potential competitors have substantially greater product development capabilities and financial, scientific, marketing and human resources than we do. Technological competition from pharmaceutical companies and biotechnology companies is intense and is expected to increase. Other companies have developed technologies that could be the basis for competitive products. Some of these products have an entirely different approach or means of accomplishing the desired therapeutic effect than products we are developing. Alternative products may be developed that are more effective, work faster and are less costly than our products. Competitors may succeed in developing products earlier than us, obtaining approvals and clearances for such products more rapidly than us, or developing products that are more effective than ours. In addition, other forms of medical treatment, such as surgery, may be competitive with our products. Over time, our technology or products may become obsolete or

uncompetitive.

### **Our Products May Not Gain Market Acceptance**

Products such as HspE7 may not gain market acceptance among physicians, patients, healthcare payors and the medical community. The degree of market acceptance of any product depends on a number of factors, including establishment and demonstration of clinical efficacy and safety, cost-effectiveness, clinical advantages over alternative products, and marketing and distribution support for the products. Limited information regarding these factors is available in connection with our products or products that may compete with ours.

Our sales experience is limited to the sale of bioreagents. To directly market and distribute any pharmaceutical products, we or our collaborators will need a marketing and sales force with appropriate technical expertise and supporting distribution capabilities. We may not be able to establish sales, marketing and distribution capabilities or enter into arrangements with third parties on acceptable terms. If we or our partners cannot successfully market and sell our products, our ability to generate revenue will be limited.

### **Our Operations and the Use of Our Products Could Subject Us to Damages Relating to Injuries or Accidental Contamination**

The human clinical trials we conduct, including trials in children, may have unforeseen long-term health implications. We have only limited amounts of product liability insurance for our clinical trials. We may not correctly anticipate or be able to maintain on acceptable terms the level of insurance coverage that would adequately cover potential liabilities from proposed clinical trials and eventual commercial sales. Product liability insurance is expensive, difficult to obtain and may not be available in the future. If we cannot obtain sufficient insurance coverage or other protection against potential product liability claims, the commercialization of our products may become financially infeasible. If any liabilities from a claim exceed the limit of insurance coverage, we may not have the resources to pay them.

Our research and development processes involve the controlled use of hazardous and radioactive materials. We are subject to federal, provincial and local laws and regulations governing the use, manufacture, storage, handling and disposal of such materials and waste products. The risk of accidental contamination or injury from handling and disposing of such materials cannot be completely eliminated. In the event of an accident involving hazardous or radioactive materials, we could be held liable for resulting damages. We are not insured with respect to this liability. Such liability could exceed our resources. In the future we could incur significant costs to comply with environmental laws and regulations.

### **Our Success Depends On Attracting and Retaining Qualified Personnel**

We depend on a core management and scientific team. The loss of any of these individuals could prevent us from achieving our business objective of commercializing our product candidates. Our future success will depend in large part on our continued ability to attract and retain other highly qualified scientific, technical and management personnel, as well as personnel with expertise in clinical testing and government regulation. We face competition for personnel from other companies, universities, public and private research institutions, government entities

and other organizations. If our recruitment and retention efforts are unsuccessful, our business operations could suffer.

### **Our Revenues Will Depend Upon the Availability of Reimbursement from Third-Party Payors That Are Increasingly Challenging the Price and Examining the Cost Effectiveness of Medical Products and Services**

Sales of therapeutic products depends in part upon the availability of reimbursement from third-party payors, including government health administration authorities, managed care providers, private health insurers and other organizations. These third-party payors increasingly attempt to contain costs by challenging the price of products and services and limiting the coverage and level of reimbursement for pharmaceutical products. Third party reimbursement for our products may be inadequate to enable us to maintain prices that provide a return on our product development investment. Governments continue to propose and pass legislation designed to reduce healthcare costs. This legislation could further limit reimbursement. If government and third-party payors do not adequately reimburse patients for the costs of our products, the market for our products may be limited.

### **Our Share Price Has Been and Is Likely to Continue to Be Highly Volatile**

As is typical for biotechnology companies without an approved product on the market, our share price has been highly volatile in the past and is likely to continue to be volatile. The price of our shares could be materially affected by factors including:

- the announcement of clinical trials results by us or our competitors
- regulatory actions
- safety issues
- changes affecting patents or exclusive licenses
- future issuances of shares
- the announcement of technological innovations
- the release of publications
- the development of new commercial products
- changes in regulations
- the release of financial results
- public concerns over risks relating to biotechnology
- sales of shares by existing shareholders and

- changes in analyst recommendations.

The volatility of our shares may be heightened while it is traded primarily on the TSX, which attracts primarily Canadian shareholders. Because some institutional investors invest in TSX-listed companies in proportion to their weight on that index, changes within the S&P/TSX Composite Index may also increase volatility in our share price. Although management continues to explore a cross-listing on the NASDAQ or a U.S. exchange, it can provide no assurances regarding the timing or ultimate results of such a transaction.

## **Item 2. PROPERTIES**

Our principal research facilities are in Victoria, British Columbia, together with our Stressgen Bioreagents Limited Partnership operations. Our two Victoria businesses share approximately 25,000 square feet of office, research and manufacturing space under a lease that expires at the end of 2005.

Most of our executive, clinical research, regulatory affairs and financial functions are provided by our subsidiary, Stressgen Biotechnologies, Inc., which has offices in San Diego, California and Collegeville, Pennsylvania. We lease approximately 10,600 square feet of office space in San Diego under a lease that expires in December 2005. Our Collegeville lease approximates 5,000 square feet and expires in December 2004. Personnel from both the parent corporation and Stressgen Biotechnologies, Inc. support the development of HspE7, for which our subsidiary Stressgen Development Corporation has primary responsibility.

## **Item 3. LEGAL PROCEEDINGS**

As of the date hereof, we are not a party to any material legal proceedings. From time to time we are involved in certain litigation arising out of our operations.

## **Item 4. SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS**

We did not submit any matters to a vote of security holders, through the solicitation of proxies or otherwise, during the quarter ended December 31, 2003.

## PART II

### Item 5. MARKET FOR REGISTRANT'S COMMON EQUITY AND RELATED STOCKHOLDER MATTERS

#### Common Share Information

Our common shares are listed and posted for trading in Canada on The Toronto Stock Exchange under the symbol "SSB." The following table sets forth, for the periods indicated, the high and low sales prices of the common shares, as reported on the Toronto Stock Exchange. All amounts following are expressed in Canadian dollars unless otherwise indicated.

	<u>High</u>	<u>Low</u>
<b>2003</b>		
Fourth Quarter	2.23	1.56
Third Quarter	2.43	1.44
Second Quarter	2.78	1.40
First Quarter	2.12	1.31
<b>2002</b>		
Fourth Quarter	2.75	1.25
Third Quarter	4.05	2.26
Second Quarter	4.59	3.25
First Quarter	5.79	3.92

On February 12, 2004, the closing price of our common shares as reported by The Toronto Stock Exchange was \$1.74 per share. We had 132 registered holders, 25 of whom were residents of the U.S. Of the approximately 72,491,000 common shares outstanding, the portion held by registered holders in the U.S. was approximately 6,554,000 or 9%.

There were approximately 13,000 holders of our common shares as of the most recent annual general meeting of shareholders on May 6, 2003.

#### Dividend Policy

We have not declared or paid any dividends on our common shares since inception. We anticipate that all available cash will be needed to finance the expansion of our business and have no plans to pay dividends in the foreseeable future.

#### Equity Compensation Plans

We have two equity compensation plans, a 1996 Share Incentive Plan and a 2001 Equity Incentive Plan. Both plans were approved by our shareholders. The following table aggregates the data from the two plans as of December 31, 2003:

Number of securities to be issued upon exercise of outstanding options (a)	Weighted-average exercise price of outstanding options (b)	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a)) (c)
4,978,118	\$4.21	358,986

### Exchange Controls and Other Limitations Affecting Holders of Common Shares

There is no law, governmental decree or regulation in Canada that restricts the export or import of capital, or which would affect our remittance of dividends or other payments to non-resident holders of our common shares, other than withholding tax requirements.

There is no limitation imposed by Canadian law or the charter or other constituent documents of Stressgen on the right of non-residents to hold or vote our common shares, other than those imposed by the *Investment Canada Act* (Canada), or the ICA.

The ICA requires each individual, government or agency thereof, corporation, partnership, trust or joint venture that is not a "Canadian" as defined in the ICA who commences a new business activity in Canada or acquires control of an existing Canadian business, where the establishment or acquisition of control is not a reviewable transaction, to file a notification with Industry Canada. The ICA generally prohibits implementation of a reviewable transaction by a non-Canadian unless after review the minister responsible for the ICA is satisfied that the investment is likely to be of net benefit to Canada. An investment in our common shares by a non-Canadian would be reviewable under the ICA if it were an investment to acquire control of Stressgen and the value of our assets of was \$5 million or more. Higher limits apply for acquisitions by or from World Trade Organization member country investors.

The acquisition of a majority of the voting interests of an entity or of a majority of the undivided ownership interests in the voting shares of an entity that is a corporation is deemed to be acquisition of control of that entity. The acquisition of less than a majority but one-third or more of the voting shares of a corporation or of an equivalent undivided ownership interest in the voting shares of the corporation is presumed to be acquisition of control of that corporation unless it can be established that, upon the acquisition, the corporation is not controlled in fact by the acquiror through the ownership of voting shares. The acquisition of less than one-third of the voting shares of a corporation or of an equivalent undivided ownership interest in the voting shares of the corporation is deemed not to be acquisition of control of that corporation. Certain transactions in relation to our common shares would be exempt from review from the ICA, including an:

- acquisition of common shares by a person in the ordinary course of that person's business as a trader or dealer in securities;

- acquisition of control of Stressgen in connection with the realization of security granted for a loan or other financial assistance and not for any purpose related to the provisions of the Investment Act; and
- acquisition of control of Stressgen by reason of an amalgamation, merger, consolidation or corporate reorganization following which the ultimate direct or indirect control in fact of Stressgen, through the ownership of voting interests, remains unchanged.

The ICA was amended with the *Act to Implement the Agreement Establishing the World Trade Organization* (Canada) to provide for special review thresholds for World Trade Organization member country investors. Under the ICA, as amended, an investment in our common shares by an investor from a country which is a member of the WTO would be reviewable only if it were an investment to acquire control of the company and the value of the assets of the company was equal to or greater than a specified amount, which increases in stages. As at December 31, 2003, the review threshold was \$223,000,000. This amount is subject to an annual adjustment on the basis of a prescribed formula in the ICA to reflect inflation and real growth within Canada.

### **Certain Canadian Federal Income Tax Information for United States Residents**

The following is a summary of certain Canadian federal income tax considerations generally applicable to holders of common shares who, for purposes of the Income Tax Act (Canada) (the "Canadian Tax Act"), deal at arm's length and are not affiliated with Stressgen, hold such shares as capital property, do not use or hold, and are not deemed to use or hold, the common shares in connection with a trade or business carried on, or deemed to be carried on, in Canada at any time, have not been at any time residents of Canada for purposes of the Canadian Tax Act and are residents of the United States of America ("U.S. Residents") under the Canada-U.S. Income Tax Convention (1980) (the "Convention"). The common shares will generally be considered to be capital property of holders unless such shares are held in the course of carrying on a business, or in an adventure or concern in the nature of trade. Furthermore, this summary does not apply to any holder which carries on an insurance business in Canada and elsewhere, in respect of the common shares that are effectively connected with the holder's Canadian insurance business or that are "designated insurance property" as defined in the Canadian Tax Act.

This summary is of a general nature only and is not intended to be, and should not be construed to be, legal, business or tax advice to any holder of common shares or prospective holder of common shares and no opinion or representation with respect to any tax consequences, including, but not limited to, Canadian federal, Canadian provincial or U.S. tax consequences, is made to any particular holder of common shares or prospective holder of common shares. Accordingly, holders of common shares and prospective holders of common shares should consult with their own tax advisers for advice with respect to the tax consequences to them having regard to their own particular circumstances, including any consequences of purchasing, owning or disposing of common shares arising under Canadian federal, Canadian provincial, U.S. Federal, U.S. state or local tax laws or tax laws of jurisdictions outside the U.S. or Canada. No advance income tax ruling has been requested or obtained from the Canada Customs and Revenue Agency to confirm the tax consequences of any of the transactions described herein.

This summary is based on the current provisions of the Canadian Tax Act and the regulations thereunder (the "Regulations"), proposed amendments to the Canadian Tax Act and/or Regulations publicly announced by the Minister of Finance (Canada) prior to the date hereof (the "Proposed Amendments"), and the provisions of the Convention as in effect on the date hereof. No assurance can be given that the Proposed Amendments will be entered into law in the manner proposed, or at all.

This summary is not exhaustive of all possible Canadian federal income tax consequences for U.S. Residents and does not take into account or anticipate any changes in law, whether by legislative, administrative, governmental or judicial decision or action, nor does it take into account Canadian provincial, U.S. or foreign tax considerations which may differ significantly from those discussed herein. No assurances can be given that subsequent changes in law or administrative policy will not affect or modify the opinions expressed herein.

A holder will not be subject to tax under the Canadian Tax Act in respect of any capital gain on a disposition or deemed disposition of common shares (including the death of the holder) unless at the time of such disposition such shares constitute taxable Canadian property of the holder for purposes of the Canadian Tax Act and such holder is not entitled to relief under an applicable tax treaty. The common shares will generally not constitute taxable Canadian property of a holder at the time of a disposition of such shares provided (1) such shares are listed on a prescribed stock exchange (which includes the Toronto Stock Exchange and would currently include the American Stock Exchange or NASDAQ), (2) the holder does not use or hold or is not deemed to use or hold, such shares in connection with carrying on a business in Canada, and (3) the holder, persons with whom such holder does not deal at arm's length, or the holder and such persons, has not owned 25% or more of the issued shares of any class or series of our share capital at any time within the 5 years preceding the date of disposition. In any event, under the Convention, gains derived by a holder who is a resident of the U.S. (within the meaning of the Convention) from the disposition of common shares will generally not be taxable in Canada unless the value of the common shares is derived principally from real property situated in Canada. If the common shares held by a holder do not constitute taxable Canadian property or if a capital gain in respect of the common shares would because of a tax treaty be exempt from tax under the Canadian Tax Act, any capital loss arising upon the disposition of the common shares will not be available to be used to offset a capital gain realized in respect of another property, which may be subject to tax under the Canadian Tax Act. To the extent the common shares disposed of constitute taxable Canadian property; the holder will be required to file a Canadian tax return, even if the gain arising from such a disposition is exempt from tax because of a tax treaty.

Amounts in respect of common shares paid or credited or deemed to be paid or credited as, on account or in lieu of payment of, or in satisfaction of, dividends to a U.S. Resident will generally be subject to Canadian non-resident withholding tax at the rate of 25%. Currently, under the Convention the rate of Canadian non-resident withholding tax will generally be reduced to: (i) 5% of the gross amount of dividends if the beneficial owner is a company (other than a limited liability company) that is resident in the U.S. and that owns at least 10% of our voting stock; or (ii) 15% of the gross amount of dividends if the beneficial owner is a resident of the U.S. (and is not a limited liability company) but does not qualify for the 5% withholding rate.

## **United States Federal Income Tax Considerations**

The following summary is a general description of the material United States federal income tax consequences of the purchase, ownership and disposition of common shares by U.S. Holders (as defined below). This summary does not address all potentially relevant U.S. federal income tax matters. This description is intended for general information purposes only and does not constitute an opinion regarding tax consequences. It is based on the United States Internal Revenue Code of 1986, as amended (the "Code"), Treasury regulations promulgated thereunder, and judicial and administrative interpretations thereof, all as in effect on the date hereof and all of which are subject to change, prospectively or retroactively.

The tax treatment of a holder of common shares may vary depending upon his particular situation. Certain holders (including, but not limited to, persons that are not U.S. Holders, banks, insurance companies, tax-exempt organizations, financial institutions, persons subject to the alternative minimum tax, real estate investment trusts, regulated investment companies, persons or entities that have a "functional currency" other than the U.S. dollar, shareholders who acquired their stock through the exercise of employer stock options, and broker-dealers) may be subject to special rules not discussed below. The following summary is limited to U.S. Holders who will hold the common shares as "capital assets" within the meaning of Section 1221 of the Code, and do not actually or constructively own 10% or more of our voting stock. The discussion below does not address the effect of any state, local or foreign tax law on a holder of the common shares.

Prospective investors should consult their own tax advisors about the federal, state, local, and foreign tax consequences of purchasing, owning and disposing of common shares.

As used herein, the term "U.S. Holder" means (i) an individual who is a citizen or resident of the United States, (ii) a partnership, corporation or other entity organized in or under (or treated for federal income tax purposes as organized in or under) the laws of the United States or any state thereof, (iii) an estate subject to United States federal income taxation without regard to the source of its income, and (iv) a trust if (a) a U.S. court is able to exercise primary supervision over the trust's administration and (b) one or more U.S. fiduciaries have the authority to control all of the trust's substantial decisions. The term "Non-U.S. Holder" shall mean the beneficial owner of common shares other than a U.S. Holder.

### ***Dividend Income***

Subject to the discussion of the "passive foreign investment company" rules below, for United States federal income tax purposes, the gross amount of a distribution with respect to common shares will include the amount of any Canadian federal income tax withheld, and will be treated as a taxable dividend to the extent of our current and accumulated earnings and profits.

To the extent that distributions exceed our current or accumulated earnings and profits, they will be treated first as a return of capital up to the U.S. Holder's adjusted basis in the common shares and thereafter as gain from the sale or exchange of the common shares.

If a dividend distribution is paid in Canadian dollars, the amounts includable in income will be the U.S. dollar value, on the date of receipt, of the Canadian dollar amount distributed. Any subsequent gain or loss in respect of such Canadian dollars arising from exchange rate fluctuations will be ordinary income or loss.

U.S. Holders who are individuals are currently subject to a maximum federal income tax rate of 15% on dividends received from foreign corporations that are "qualified foreign corporations", as defined by the Code. We believe that the Company is a qualified foreign corporation.

Subject to the limitations set forth in the Code, as modified by the United States-Canada income tax treaty, U.S. Holders may elect to claim a credit against their United States federal income tax liability for Canadian income tax withheld from dividends received in respect of common shares. For purposes of calculating the credit for the Canadian taxes paid against the United States taxes imposed, the dividend should be foreign source income. The rules relating to the determination of the foreign tax credit are complex. U.S. Holders should consult their personal tax advisors to determine whether and to what extent they would be entitled to such credit. U.S. Holders that do not elect to claim foreign tax credits may instead claim a deduction for Canadian income tax withheld.

### *Sale of Common Stock*

Subject to the discussion of the "passive foreign investment company" rules below, the sale of common shares will generally result in the recognition of gain or loss in an amount equal to the difference between the amount realized on the sale and the holder's adjusted basis in such common shares.

Gain or loss upon the sale of the common shares will be long-term or short-term capital gain or loss, depending on whether or not the common shares were held for more than one year prior to the sale. Preferential tax rates for long-term net capital gains are applicable to a U.S. Holder that is an individual, estate or trust. There are currently no preferential tax rates for long-term capital gains for a U.S. Holder that is a corporation. Short-term capital gains are generally taxed at ordinary income tax rates. Deductions for net capital losses are subject to significant limitations.

### *PFIC Status*

Special rules are applicable to U.S. Holders that hold stock of a "passive foreign investment company" ("PFIC"). A foreign corporation is a PFIC if at least 75% of its gross income for the taxable year is passive income or if at least 50% by value of the assets it holds during the taxable year produce or are held for the production of passive income. For publicly traded corporations such as Stressgen, the asset test is met if the fair market value of passive income-producing assets equals or exceeds 50% of the sum of the corporation's liabilities plus the value of its outstanding stock. U.S. Holders of common shares can be adversely affected by the PFIC rules if they hold or have held our common shares in a year in which we have or had PFIC status.

In general, a U.S. Holder of common shares in a PFIC is required to prorate all gains realized on the disposition of such U.S. Holder's common shares and all "excess distributions" (as such term

is defined by Section 1291) over the entire holding period for the common shares (excluding any period prior to the first year during which we were a PFIC). All gains or excess distributions allocated to such prior years are taxed at the highest tax rate for each such prior year applicable to ordinary income. The U.S. Holder also would be liable for interest on the foregoing tax liability for each such prior year calculated as if such tax liability had come due in each such prior year. However, if the U.S. Holder makes a timely election to treat a PFIC as a qualified electing fund ("QEF") with respect to such holder's interest therein, the above-described rules generally will not apply. Instead, the electing U.S. Holder would include annually in his gross income his pro rata share of the PFIC's ordinary earnings and net capital gain regardless of whether such income or gain was actually distributed. A U.S. Holder of a QEF can, however, elect to defer the payment of U.S. federal income tax on such income inclusions, but would then be obligated to interest to the government on the deferred payment. In addition, subject to certain limitations, U.S. Holders owning marketable stock in a PFIC are permitted to elect to mark that stock to market annually. Amounts included in or deducted from income under the mark to market alternative (and actual gains and losses realized upon disposition, subject to certain limitations) will be treated as ordinary gains or losses.

We believe that Stressgen was not a PFIC for the year 2003 or prior years. However, because PFIC status depends on the character of our income and assets in each year, there can be no assurance with respect to whether we will qualify as a PFIC in future years. Further, there can be no assurance that our determination concerning our PFIC status will not be challenged by the IRS. If we determine that Stressgen is a PFIC we will determine at that time whether we will provide sufficient information for a U.S. Holder to make the QEF election. Therefore, each prospective investor is urged to consult with a tax advisor with respect to how the PFIC rules would affect its tax situation.

#### ***Controlled Foreign Corporation Status***

If more than 50% of the voting power of all classes of stock or the total value of our stock is owned, directly or indirectly, by citizens or residents of the United States, United States domestic partnerships and corporations or estates or trusts other than foreign estates or trusts, each of whom own 10% or more of the total combined voting power of all classes of stock of the Company ("10% U.S. Shareholders"), Stressgen could be treated as a CFC under Subpart F of the Code. If in 1998 or thereafter Stressgen qualifies as a CFC, 10% U.S. Shareholders are generally not required to apply the PFIC rules, provided that, in some cases, complex tax elections are made. The classification of Stressgen as a CFC would effect many complex results including the required inclusion by 10% of U.S. Shareholders' in income of their pro rata shares of our Subpart F income. In addition, gain from the sale or exchange of stock by a holder of our shares who is or was a 10% U.S. Shareholder at any time during the five-year period ending with the sale or exchange is treated as ordinary dividend income to the extent of our earnings and profits attributable to the stock sold or exchanged. Because of the complexity of Subpart F, and because it is not clear that Subpart F would apply to the holders of our shares, a 10% U.S. Holder is urged to consult with their tax advisors to determine the applicable rules.

Due to the complexity of the tax rules, U.S. persons who are shareholders of Stressgen are strongly urged to consult their own tax advisors concerning the impact of these rules on their investment in our shares.

### **Changes in Securities**

In December 2003, we issued a total of 10,638,298 units in a Canadian offering which was exempt from U.S. registration requirements under Regulation S. Each unit was comprised of one common share and one-half of one purchase warrant. Each whole warrant entitles the holder to purchase one additional common share for a period of 36 months from December 23, 2003 at a price of \$2.44 per common share. The offering was made by a syndicate of underwriters co-led by Canaccord Capital Corporation and Raymond James Ltd. and including Desjardins Securities Inc., Orion Securities Inc. and Dlouhy Merchant Group Inc. The units were issued at the price of \$1.88 each, for net proceeds of approximately \$18,700,000.

We paid to the underwriters and incurred share issue costs of approximately \$1,300,000 in consideration of services rendered by them in connection with the offering. We also agreed to indemnify the underwriters and their broker/dealer affiliates against certain liabilities, including liabilities under the United States securities laws and under Canadian securities legislation and to contribute to payments that the underwriters may be required to make in respect thereof. In addition, we agreed not to issue or enter into agreement to issue any common shares or any securities convertible into or exchangeable for common shares without the prior consent of the underwriters, such consent not to be unreasonably withheld, until the date which is 90 days after the closing of the offering, except pursuant to our stock option plan, employee purchase plans and any convertible securities that are outstanding on the date hereof

We intend to use the net proceeds of the financing primarily for general corporate purposes, including for the manufacturing and clinical development of HspE7 and working capital.

## **Item 6. SELECTED FINANCIAL DATA**

### **Annual Financial Data**

Our consolidated financial statements have been prepared in accordance with generally accepted accounting principles in Canada ("Canadian GAAP"). These principles differ in certain respects from generally accepted accounting principles in the United States of America ("U.S. GAAP"). The differences as they affect our financial statements are described in Note 11 to our audited consolidated financial statements filed as part of Item 8 hereof. Because we report on a consolidated basis, our results include those of our subsidiaries, including a U.S. subsidiary, which provides management, research and development services, and a Barbados subsidiary, which is responsible for the development of HspE7.

## Consolidated Statement of Operations Data

	Year ended December 31				
	2003	2002	2001	2000	1999
	(In thousands of Canadian dollars, except per share amounts)				
Net revenues					
Canadian and U.S. GAAP .....	\$13,419	\$14,042	\$5,419	\$4,156	\$3,274
Research and development expenses					
Canadian and U.S. GAAP .....	20,865	33,675	35,906	23,961	14,322
Net loss <sup>(1)</sup>					
Canadian GAAP.....	(16,245)	(28,802)	(35,939)	(25,407)	(16,738)
U.S. GAAP.....	(15,298)	(28,922)	(36,341)	(35,766)	(19,515)
Basic and diluted loss per common share					
Canadian GAAP.....	(0.26)	(0.49)	(0.70)	(0.63)	(0.58)
U.S. GAAP.....	(0.25)	(0.49)	(0.71)	(0.88)	(0.67)

## Consolidated Balance Sheet Data

	As of December 31				
	2003	2002	2001	2000	1999
	(In thousands of Canadian dollars)				
Cash and short-term investments					
Canadian GAAP.....	\$52,090	\$46,013	\$62,682	\$70,567	\$16,477
U.S. GAAP.....	52,090	46,013	62,682	70,710	16,477
Total assets <sup>(2)</sup>					
Canadian GAAP.....	56,430	54,815	67,789	74,325	19,852
U.S. GAAP.....	56,430	54,815	67,789	74,468	19,852
Long-term obligations					
Canadian GAAP.....	2,672	3,606	578	1,036	1,467
U.S. GAAP.....	2,672	3,606	578	1,036	1,467

The information set forth above is not necessarily indicative of the results of future operations and should be read in conjunction with the consolidated financial statements and related notes thereto and with "Management's Discussion and Analysis of Financial Condition and Results of Operations" included as part of this Form 10-K.

- (1) To conform with U.S. GAAP, our net loss would decrease by \$947,000 in 2003 and increase by \$120,000 in 2002, \$402,000 in 2001, \$10,359,000 in 2000, and \$2,777,000 in 1999. In 2003, the

principal difference in our net loss under U.S. GAAP rather than Canadian GAAP was due to the reversal of \$541,000 in unrealized foreign exchange losses and the reversal of a \$406,000 previously recorded adjustment to short-term investments. In 2002, the principal difference in our net loss under U.S. GAAP rather than Canadian GAAP was due to the reversal of \$69,000 in unrealized foreign exchange gain and the reversal of a \$51,000 previously recorded adjustment to short-term investments. In 2001, the principal difference in our net loss under U.S. GAAP rather than Canadian GAAP was due to unrealized foreign exchange gain on available for sale securities of \$541,000 offset by net \$139,000 of other items. In 2000, the principal difference in our net loss was due to the release of escrow shares of \$9,093,000, stock based compensation expenses including non-compensatory costs to non-employees of \$1,674,000, and changes related to unrealized losses on available for sale securities totaling \$372,000. In 1999, the principal difference was due to the release of escrow shares totaling \$2,061,000 and a net loss of \$768,000 resulting from the dissolution of the joint venture.

- (2) At December 31, 2003, 2002, 2001 and 1999, there were no differences in total assets under U.S. GAAP relative to Canadian GAAP. At December 31, 2000, the difference in total assets under U.S. GAAP relative to Canadian GAAP was \$143,000, due to an increase in market value on available-for-sale securities.

### Currency Exchange Rates

Our accounts are maintained in Canadian dollars. In this Annual Report on Form 10-K, all dollar amounts are stated in Canadian dollars except where otherwise indicated.

The table below shows relevant exchange rates which approximate the noon buying rates in New York City as reported by the Federal Reserve Bank of New York for cable transfers expressed in Canadian dollars for our five most recent fiscal years. The average rate means the average of the exchange rates on the last day of each month during a year.

Fiscal Year Ended December 31,

	2003	2002	2001	2000	1999
High	\$1.5747	\$1.6128	\$1.6023	\$1.5600	\$1.5302
Low	1.2924	1.5108	1.4933	1.4350	1.4440
Average	1.4015	1.5702	1.5518	1.4855	1.4858
Period End	1.2924	1.5800	1.5925	1.4995	1.4440

As of February 12, 2004, the noon buying rate in New York City for cable transfers in Canadian dollars as certified for customs purposes by the Federal Reserve Bank of New York was U.S.\$0.76 = Cdn.\$1.00 (equivalent to U.S.\$1.00 = Cdn.\$1.3191).

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

The Management's Discussion and Analysis of Financial Condition and Results of Operations contains forward-looking statements that involve risk and uncertainties. The predictions described in these statements may not materialize if management's current expectations regarding our future performance prove incorrect. Our results could also be affected by factors including, but not limited to, our reliance on collaborative partners and other risks described

above under "Factors That May Affect Future Performance." The forward-looking statements are based on currently available information; we disclaim any obligation to update them.

The following information should be read in conjunction with our 2003 consolidated financial statements and related notes therein, which are prepared in accordance with Canadian GAAP. These principles differ in certain respects from U.S. GAAP. The differences, as they affect our consolidated financial statements, are described in Note 11 to our consolidated financial statements. All amounts following are expressed in Canadian dollars unless otherwise indicated.

## **Overview**

From our inception in 1990 to 1993, our core business involved the sale of bioreagents. Although we have retained and expanded our bioreagent business worldwide, our primary focus since 1993 has been the research and development of innovative stress protein-based fusion products that will stimulate the body's immune system to combat viral infections and related cancers. Our core, exclusively licensed technology involves the fusion of heat shock proteins with viral or cancer-associated antigens. The lead product candidate developed with this technology, HspE7, targets a variety of human papillomavirus-related diseases. We are also performing research studies on potential treatments for hepatitis B and herpes simplex and are evaluating whether our technology could produce a fusion protein to treat infections caused by hepatitis C.

We have incurred significant losses since our inception and expect to incur substantial losses for the foreseeable future as we invest in our research and product development programs, including manufacturing, pre-clinical studies and clinical trials, and regulatory activities. At December 31, 2003 our accumulated deficit was \$150,294,000. Historically, we have depended principally on equity financings to fund our business activities. We intend to pursue additional equity financings to fund our business activities, markets permitting.

During the period encompassed herein, we have devoted over 60% of our resources to our HspE7 product development program. HspE7 is being developed as a treatment for conditions caused by HPV, including genital warts, recurrent respiratory papillomatosis, anal intraepithelial neoplasia, cervical intraepithelial neoplasia and cervical cancer. The balance of our resources were devoted to our on-going research programs involving the fusion of heat shock proteins with viral or cancer associated antigens and research in support of our bioreagent business.

Our success depends upon the safety and efficacy of our products in pre-clinical studies and clinical trials, and also on obtaining the necessary regulatory approvals to market our products. The marketability of our products will be influenced by competition from alternative therapies and the degree of protection our intellectual property provides. We will also need to recruit and retain personnel skilled in the product development process to obtain our objectives. We believe there will be significant markets for our therapeutic products should these products prove to be effective in human clinical trials.

### *Restructured Roche Agreement*

On December 2, 2003, we announced a restructuring of our June 24, 2002 collaboration agreement with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. (together, "Roche"), providing for the development and commercialization of our pharmaceutical fusion product candidate, HspE7. By regaining control of the HspE7 manufacturing program, we expect the restructured agreement to better facilitate our clinical development of HspE7 in recurrent respiratory papillomatosis and additional indications caused by the human papillomavirus, while allowing Roche to develop a second generation HspE7 product targeting genital warts. We have resumed all responsibility for all manufacturing and other costs of the indications we choose to develop.

Roche may pay a fee and event-driven milestones aggregating up to \$207,000,000 (US\$138,000,000) to obtain exclusive rights to the first generation HspE7 product, in which case it will become responsible for related costs. Assuming this fee is paid and all HspE7 development and commercial milestones are achieved and Roche exercises its rights to certain other CoVal™ fusion product candidates, the payments to us, excluding sales-based payments (similar to royalties), could approximate \$340,500,000 (U.S.\$227,000,000), beyond the approximately \$32,250,000 (U.S.\$21,500,000) we have received from Roche relating to the development of a first generation HspE7 product to date. Until March 31, 2005 we can elect, under defined circumstances, to terminate Roche's exclusive rights to the first generation HspE7 product.

Once the first generation HspE7 product is on the market, we can elect to launch a sales force in the U.S. and Canada and record sales for three years after regulatory approval in those countries. In that case we will pay Roche a mid-single digit percentage or a low double-digit percentage of our net sales, depending upon the timing and occurrence of Roche's exercise. Under these conditions, no earlier than three years after market launch of HspE7, Roche can begin recording sales in the U.S. and Canada. Once Roche begins recording sales in those countries, we will receive sales-based payments, which are expected to approximate 35% of Roche's net HspE7 product sales. In the rest of the world, Roche will record sales immediately after market launch and we will receive sales-based payments of 20% of Roche's net sales.

Roche can also obtain exclusive rights to develop a second generation HspE7 product upon payment of a license fee. In such case, we will receive alternative milestones based upon the clinical and regulatory development of the second generation product. Roche will assume responsibility for manufacturing and all costs of its development program. After commercialization of the second generation HspE7 product, we will receive tiered, progressive sales-based payments from Roche at levels that we believe are competitive with other agreements of this stage and type. Roche can credit a portion of its milestone payment against the sales-based payments on the second generation product.

Roche is obligated to make additional commercial success payments of up to \$127,500,000 (US\$85,000,000) depending upon the aggregate net sales of either or both generations of the HspE7 product. In addition Roche has separate non-exclusive rights to negotiate licenses to our CoVal™ fusion product candidates for the treatment of cancer and hepatitis C. By paying additional fees, Roche can make these rights exclusive to January 1, 2007.

## Liquidity and Capital Resources

Since inception we have relied principally on equity financings, coupled with cash flows generated from our bioreagents business, to fund our research and development programs, operations and capital expenditures. Through December 31, 2003 we have raised net equity proceeds of \$199,056,000, including approximately \$18,700,000 of net proceeds from an equity financing in December 2003.

Under the terms of our restructured collaboration agreement with Roche, we may receive approximately \$15,000,000 to \$22,500,000 (US\$10,000,000 to US\$15,000,000) in 2005. We have assumed responsibility for all manufacturing costs of producing first generation HspE7 product along with any additional incremental costs of pursuing the indications we choose to develop, including RRP. At this time, we do not have internal manufacturing capabilities to supply material for clinical trials or provide commercial quantities of HspE7 and therefore we will need significant additional funds. If adequate funds are not available, we may be required to delay, reduce the scope of, or eliminate the development of HspE7 or other research or development programs.

We believe that our current capital resources are sufficient to fund operations into 2005. This belief is based on our research and development plans, the current regulatory environment, our historical industry experience in the development of therapeutics and general economic conditions.

We employ a financial performance measurement system designed to ensure our revenues and expenses are consistent with management's operational objectives and budgetary constraints. Our cash utilization in 2004 is dependent upon several factors, including the timing and progress of clinical development of HspE7 and the cost of manufacturing clinical supplies.

At December 31, 2003, we had \$52,090,000 of cash, cash equivalents and short-term investments. The \$6,077,000 increase over 2002 is due principally to \$18,700,000 raised through an equity financing along with \$4,594,000 of net proceeds from an equity investment by Roche, offset by net losses of \$16,245,000. At December 31, 2003 and 2002, approximately 24% and 13% of cash, cash equivalents and short-term investments were held in U.S. dollars.

During 2003, capital expenditures totaled \$165,000 compared with \$380,000 and \$1,783,000 during 2002 and 2001 respectively. The 2003 reduction in capital spending is due to management's investment policy limiting purchases to those required to preserve our current level of manufacturing and research capabilities. The 2002 reduction in capital expenditures compared to 2001 was due to the completion of significant improvements to our laboratory facilities and additional purchases of laboratory equipment to support our ongoing research and bioreagent manufacturing activities in 2001. Capital expenditures during 2004 are expected to remain consistent at 2003 levels, reflecting management's strategic investment policy.

At December 31, 2003 and 2002 we had outstanding principal balances of, \$1,125,000 and \$580,000, respectively, in the form of fixed rate capital leases and term loan agreements. In September 2003 we entered into a term loan agreement with Oxford Finance Corporation,

collateralized by equipment we own. At December 31, 2003 there was \$906,000 outstanding on the loan. Under the terms of the agreement, we must issue a letter of credit for the outstanding loan balance if combined cash, cash equivalents, and short-term investments fall below \$6,000,000.

The following table summarizes our contractual obligations as of December 31, 2003. The table does not include items such as contracts with outside parties as the commitment to pay does not exist until completion of work.

Contractual Obligations	Payments due by period (including interest)				
	Total	Less than 1 year	1 – 3 years	3 – 5 years	More than 5 years
Term loan	\$1,040,000	\$440,000	\$600,000	--	--
Capital lease obligations	\$231,000	\$176,000	\$55,000	--	--
Operating lease obligations	\$1,694,000	\$875,000	\$819,000	--	--

We will require additional capital to fund future research and product development activities. We expect to seek additional funds from various sources, including corporate partners that enter into research and development collaborations with us, and public and private equity financings. We cannot assure you that additional financing will be available when needed or on satisfactory terms. If we raise additional funds by issuing equity securities, substantial dilution to our existing shareholders may result. We may need to obtain funds through collaborative arrangements with others that are on unfavorable terms. We may also have to relinquish rights to certain of our technologies, product candidates or products that we would otherwise seek to develop ourselves.

### **Results of Operations**

During 2003, we realized a net loss of \$16,245,000 or \$ 0.26 per common share. These results compare with a net loss of \$28,802,000 in 2002 and \$35,939,000 in 2001 (\$0.49 and \$0.70 per share, respectively). The \$12,557,000 improvement in our net loss position during 2003 compared to 2002 is due principally to decreased spending on research and development (“R&D”) activities related to manufacturing development spending that was funded by Roche, along with the timing of expenses related to our ongoing clinical trials.

### ***Collaborative R&D revenue***

We recorded collaborative R&D revenue of \$8,094,000 and \$8,370,000 in 2003 and 2002, respectively, relating to development activities in support of Roche’s activities under the June 2002 collaboration agreement and amortization of up-front license fees in accordance with Staff Accounting Bulletin (“SAB”) No 101 “Revenue Recognition in Financial Statements.” Collaborative R&D revenue in 2003 includes \$4,912,000 for development activities, \$2,214,000

for a time based milestone payment and \$968,000 for the amortization of upfront license fees. Collaborative R&D revenue in 2002 includes \$7,815,000 for development activities and \$555,000 from the amortization of upfront license fees. Under the terms of the restructured HspE7 collaboration agreement, we expect future collaborative R&D revenue to include amortization of the initial up-front license fee, which was adjusted to reflect the increased development period, and recognition of future milestone revenues.

### ***Bioreagent sales***

The production and sale of bioreagents supports our business strategy by building our market presence in stress proteins and strengthening our strategic relationships with companies, academic institutions and stress response researchers. Our products are sold directly to end-users and through third party distributors. In 2003, an overall economic slowdown in North America caused industry-wide demand for bioreagents to slow. These events combined with the weakening U.S. dollar compared to the Canadian dollar, decreased our 2003 bioreagent sales by 6% to \$5,325,000 compared to 2002. The effect of the weakening U.S. dollar on our reported sales results totaled approximately \$625,000 for the year ended December 31, 2003. These impacts were partially offset by the introduction of several higher priced kit-based research products. Our bioreagent sales increased by 5% in 2002, compared to 2001, attributed principally to increased demand for stress protein and antibody bioreagents, increased prices and complementary new product introductions.

### ***Research and development***

Research and development, or R&D, includes costs associated with clinical studies, product development, and ongoing exploratory research. In order to optimize our financial flexibility, we employ clinical research organizations to conduct our clinical trials and engage contract manufacturers to assist us with product development and manufacturing.

R&D spending decreased by approximately 38% to \$20,865,000 in 2003, compared with \$33,675,000 in 2002. The 2003 decrease is due to the reduction in manufacturing development spending and timing of expenses recorded for our on-going clinical trials as compared to 2002. During 2002, R&D spending decreased by approximately 6% to \$33,675,000, compared with \$35,906,000 in 2001. The 2002 decrease reflects a mid-2002 cost shift of HspE7 manufacturing scale-up costs and other product development efforts to Roche under the now superseded June 2002 Roche collaboration agreement.

Our R&D spending in 2003 consisted principally of in-house research activities, spending to support the final stages of our clinical trials, and activities to support our collaboration with Roche. During 2003, our clinical program focused on our RRP phase II trial and AIN phase III trials. We released interim data on the RRP phase II trial in 2003. Final data related to both the RRP and AIN trials is expected in 2004. During 2003 over 60% of our R&D spending related to efforts developing HspE7 as compared with over 80% in 2002. The remaining spending related to exploratory research focusing on our follow-on CoVal<sup>TM</sup> fusion product candidates and research in support of our bioreagent business. During 2004, we expect to devote approximately 90% of planned R&D spending to support HspE7 development. We anticipate that R&D

spending will increase in 2004 due to our assumption of HspE7 manufacturing and development activities from Roche and preparation for additional clinical trials.

### ***Selling, general and administrative expenses***

Selling, general and administrative expenses, or SG&A, includes executive management, business development, investor relations, legal support and general administration.

SG&A expenses decreased by 13% to \$7,303,000 in 2003 compared with \$8,409,000 in 2002, and \$7,782,000 in 2001. The fluctuations between 2003, 2002, and 2001 are due principally to increased 2002 spending on business development activities associated with consummating our original collaboration agreement with Roche. We anticipate that in 2004 SG&A spending will be consistent with that of 2003.

### ***Cost of bioreagent sales***

The aggregate cost of bioreagent sales as a percentage of bioreagent sales was approximately 25% in 2003 and 29% in 2002 and 2001, resulting in gross margins of 75% in 2003 and 71% in 2002 and 2001. The 2002 and 2001 gross margins were lower than in 2003 due principally to write-offs of obsolete and slow moving inventory. We continually review sales trends in determining the realizable value of inventories and make adjustments, as necessary. In 2004, we anticipate that the gross margin will be between 72% and 76%.

### ***Interest and other income***

Interest and other income decreased in 2003 by 45% to \$702,000 compared with \$1,267,000 in 2002. Lower market interest rates applied to a lower investment portfolio balance contributed to the decline. Also, a temporary loss of market value on investments was recorded in 2003, which is expected to reverse in the first half of 2004.

Interest and other income decreased by 49% to \$1,267,000 in 2002 compared with \$2,507,000 in 2001. Our reduced cash and short term investment balances and lower interest rates available in 2002, compared to 2001, resulted in less interest income.

### ***Net foreign exchange gain/loss***

In 2003 foreign exchange loss increased by 158% to \$833,000 from \$323,000 in 2002. During the past two years, the U.S. and Canadian dollar exchange rate has fluctuated dramatically, causing gains and losses from quarter to quarter. We have reduced this foreign exchange volatility, in part, by ensuring that the majority of our investments are denominated in Canadian dollars.

In 2002 we incurred a \$323,000 loss compared to a \$1,502,000 gain in 2001. This loss resulted from the volatility of currency markets and the weakening of the U.S. dollar compared to the Canadian dollar during 2002.

### ***Basic and diluted loss per share***

The 44% decrease in net loss to \$16,245,000 in 2003 compared with \$28,802,000 in 2002, was diluted by a 4% increase in the weighted average number of common shares outstanding, resulting in basic and diluted loss per share of \$0.26 in 2003 and \$0.49 in 2002.

The 20% decrease in net loss to \$28,802,000 in 2002, compared with \$35,939,000 in 2001, was diluted by a 15% increase in the weighted average number of common shares outstanding, resulting in basic and diluted loss per share of \$ 0.49 in 2002, compared with \$0.70 in 2001.

### ***Differences between Canadian and U.S. generally accepted accounting principles***

Our financial statements have been prepared in accordance with Canadian GAAP. Certain adjustments would be required if these statements were to be prepared in all material respects in accordance with U.S. GAAP.

To conform to U.S. GAAP, our net loss would decrease by \$947,000 in 2003 and increase by \$120,000 in 2002 and \$402,000 in 2001. In 2003, the principal difference in our net loss using U.S. GAAP rather than Canadian GAAP is due to the reversal of an unrealized foreign exchange loss on available-for-sale securities of \$541,000, coupled with a \$406,000 reversal of previous adjustments to short-term investments. Under U.S. GAAP, adjustments to the market value of our investment portfolio would be recorded as a component of stockholders' equity. Under Canadian GAAP, unfavorable market value adjustments are recorded as a component of retained earnings.

Similarly, in 2002, the principal difference in our net loss using U.S. GAAP rather than Canadian GAAP is due to the reversal of \$69,000 in unrealized foreign exchange gain on available for sale securities and a \$51,000 reversal of market value adjustments previously made to short term investments recorded under Canadian GAAP. In 2001, the principal difference in our net loss using U.S. GAAP rather than Canadian GAAP is due to the reversal of \$541,000 in unrealized foreign exchange gain recorded under Canadian GAAP. A complete discussion of these and other less significant differences between U.S. GAAP and Canadian GAAP are described in Note 11 to our consolidated financial statements.

Net loss per common share under U.S. GAAP would have been \$0.25, \$0.49 and \$0.71 in 2003, 2002 and 2001, respectively. There are no differences under Canadian and U.S. GAAP with respect to our current assets and our stockholders' equity at December 31, 2003 and 2002.

### **Critical Accounting Policies**

Our significant accounting policies are disclosed in Note 1 to our consolidated financial statements. Certain of our policies require the application of management judgment in making estimates and assumptions that affect the amounts reported in the consolidated financial statements and disclosures made in the accompanying notes. Those estimates and assumptions are based on historical experience and various other factors deemed applicable and reasonable under the circumstances. The use of judgment in determining such estimates and assumptions is, by nature, subject to a degree of uncertainty. Accordingly, actual results could differ from the estimates made. Our critical accounting policies include:

### ***Revenue recognition***

Revenue from collaborative R&D arrangements may include multiple elements within a single contract. Our accounting policy complies with the revenue determination requirements set forth in EITF 00-21 "Accounting for Revenue Arrangements with Multiple Deliverables," and EIC 142 "Revenue Arrangements with Multiple Deliverable," relating to the separation of multiple deliverables into individual accounting units with determinable fair values. We have estimated the fair value of deliverables in the Roche agreement using standard industry techniques. Changes in the determination of fair values or performance periods relating to certain deliverables, and associated milestones, could impact the timing of future revenue streams.

### ***Clinical trial accruals***

Clinical trial costs constitute a significant portion of R&D expense. We recognize expenses related to our ongoing clinical trials using a methodology designed to accrue estimated costs in the appropriate accounting periods. Clinical trials can span multiple accounting periods. We recognize clinical trial costs in three distinct phases: start-up phase, patient accrual phase, and close-out phase. Our expenses related to clinical trials could vary based on patient availability, additional statistical analysis requirements, and decisions to extend the patient evaluation period. Using our current trial accrual methodology, our liability for clinical trials as of December 31, 2003 is \$1,409,000, including the estimated effect of any work-in-process terminated at the end of the reporting period. Alternately, if we utilized a percentage of completion approach and used an operational estimate of the actual work completed as of December 31, 2003 compared to the total contract value, our clinical trial liability would decrease by approximately \$270,000.

### ***Stock-based compensation***

In September 2003, the CICA Accounting Standards Board released revised transitional provisions for *Stock-Based Compensation and Other Stock-Based Payments*, Section 3870, to provide the same alternative methods of transition as is provided in the U.S. for voluntary adoption of the fair value based method of accounting. The AcSB has also amended Section 3870 to require that all transactions whereby goods and services are received in exchange for stock-based compensation and other payments result in expenses that should be recognized in financial statements, and that this requirement would be applicable for financial periods beginning on or after January 1, 2004. Section 3870 requires that share-based transactions should be measured on a fair value basis. The Company will adopt the provisions of AcSB Section 3870 beginning January 1, 2004.

## **Item 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK**

We use the Canadian dollar as our measurement and functional currency. As a result, we are exposed to foreign currency fluctuations through our operations because a substantial amount of our contract research and development spending has been transacted in other currencies, principally in U.S. dollars. However, since approximately 95% of our bioreagent product sales are in U.S. dollars, there is partial matching of U.S. dollar denominated expenses and revenues. We translate monetary assets and liabilities into Canadian dollars using the rate of exchange prevailing at our balance sheet date. We record the resulting exchange gains and losses in our

statement of operations. Although we do not currently engage in hedging or other activities to reduce foreign currency risk, beyond matching investments proportionately with anticipated spending, we may do so in the future if conditions change.

A hypothetical change in foreign exchange rates by applying a 10% change to our year-end foreign exchange rate, then applying that rate to our average level of U.S. investments during the year, would result in a \$286,000 impact. If the value of the Canadian dollar relative to the U.S. dollar were to increase by 10%, our net loss would decrease by \$286,000. Further, if the value of the Canadian dollar relative to the U.S. dollar were to decrease by 10%, our net loss would increase by \$286,000.

We are also exposed to interest rate risk, because we maintain cash equivalent and short-term investment portfolio holdings of various issuers, types, and maturity dates with large banks and investment banking institutions. We occasionally hold short-term investments beyond 120 days. The market value of these short-term investments on any day during the investment term may vary as a result of market interest rate fluctuations.

A hypothetical change in interest rates comparable to a 10% change to our average rate of return would result in a \$77,000 impact. If interest rates were to increase by 10%, our net loss would decrease by \$77,000. Further, if interest rates were to decrease by 10%, our net loss would increase by \$77,000.

We have not used derivative financial instruments in our investment portfolio. We classify our investments as available-for-sale or held-to-maturity at the time of purchase and re-evaluate this designation as of each balance sheet date. We had \$52,090,000 in cash, cash equivalents and short-term investments as of December 31, 2003.

## **Item 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA**

### **REPORT OF MANAGEMENT**

Management is responsible for the preparation of the consolidated financial statements and all related information appearing in this Annual Report. The consolidated financial statements and notes have been prepared in conformity with Canadian generally accepted accounting principles and include certain amounts that are estimates based upon currently available information and management's judgment of current conditions and circumstances.

To provide reasonable assurance that assets are safeguarded against losses from unauthorized use or disposition and that accounting records are a reliable source for financial statement preparation, management maintains a system of accounting and other controls. Even an effective internal control system, no matter how well designed, has inherent limitations – including the possibility of circumvention or overriding of controls – and therefore can provide only reasonable assurance with respect to financial statement presentation. We seek to improve and modify our internal control system in response to changes in business conditions, operations and prevailing practices and recommendations made by our independent auditors.

The Audit Committee of the board of directors, which is composed of independent directors, meets periodically with management, and the independent auditors to review auditing, internal controls and financial reporting matters. The independent auditors periodically meet with the Audit Committee and have access to its individual members.

The Company engaged Deloitte & Touche LLP, independent accountants, to audit the consolidated financial statements in accordance with auditing standards generally accepted in Canada and the United States of America, which includes consideration of the internal control structure.

/s/ Daniel L. Korpolinski  
President and Chief Executive Officer

/s/ Gregory M. McKee  
Vice President of Corporate Development  
and Chief Financial Officer

## INDEPENDENT AUDITORS' REPORT

To the Stockholders of Stressgen Biotechnologies Corporation:

We have audited the accompanying consolidated balance sheet of Stressgen Biotechnologies Corporation and subsidiaries (the "Company") as of December 31, 2003 and 2002 and the related consolidated statements of operations, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2003. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with auditing standards generally accepted in Canada and 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, such consolidated financial statements present fairly, in all material respects, the financial position of Stressgen Biotechnologies Corporation and subsidiaries as of December 31, 2003 and 2002 and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2003 in accordance with accounting principles generally accepted in Canada.

/s/ Deloitte & Touche LLP

February 12, 2004  
San Diego, California

**STRESSGEN BIOTECHNOLOGIES CORPORATION**  
**CONSOLIDATED BALANCE SHEET**  
(Canadian dollars in thousands, except share information)

	<u>December 31,</u> <u>2003</u>	<u>December 31,</u> <u>2002</u>
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 19,996	\$ 31,202
Short-term investments	32,094	14,811
Accounts receivable, net	733	4,279
Inventories	639	838
Other current assets	512	518
Total current assets	53,974	51,648
Plant and equipment	2,196	2,746
Deferred expenses, net of current portion	260	421
	\$ 56,430	\$ 54,815
<b>Liabilities and Stockholders' Equity</b>		
Current liabilities:		
Accounts payable and accrued liabilities	\$ 3,975	\$ 8,833
Current portion of deferred revenue	688	1,115
Current portion of notes payable	518	318
Total current liabilities	5,181	10,266
Long-term liabilities:		
Deferred revenue, net of current portion	2,065	3,344
Notes payable, net of current portion	607	262
Total long-term liabilities	2,672	3,606
Total liabilities	7,853	13,872
Stockholders' equity:		
Common shares and other equity – no par value; unlimited shares authorized, 72,491,403 and 60,209,989 shares issued and outstanding at December 31, 2003 and 2002, respectively	199,056	175,384
Deferred stock compensation	(185)	(392)
Accumulated deficit	(150,294)	(134,049)
Total stockholders' equity	48,577	40,943
	\$ 56,430	\$ 54,815

See accompanying notes to consolidated financial statements

/s/ DANIEL L. KORPOLINSKI  
Director, President and Chief Executive Officer

/s/ KEN GALBRAITH  
Director

# STRESSGEN BIOTECHNOLOGIES CORPORATION

## CONSOLIDATED STATEMENT OF OPERATIONS

(Canadian dollars in thousands, except per share amounts)

	Years ended December 31,		
	2003	2002	2001
Revenue:			
Collaborative R&D revenue	\$ 8,094	\$ 8,370	\$ -
Bioreagent sales	5,325	5,672	5,419
Total revenue	13,419	14,042	5,419
Operating expenses:			
Research and development	20,865	33,675	35,906
Selling, general and administrative	7,303	8,409	7,782
Cost of bioreagent sales	1,312	1,635	1,573
	29,480	43,719	45,261
Operating loss	(16,061)	(29,677)	(39,842)
Other income (expenses):			
Interest and other income	702	1,267	2,507
Net foreign exchange (loss) gain	(833)	(323)	1,502
Interest expense	(53)	(69)	(106)
	(184)	875	3,903
Net loss	\$ (16,245)	\$ (28,802)	\$ (35,939)
Basic and diluted loss per common share	\$ (0.26)	\$ (0.49)	\$ (0.70)
Weighted average shares used to compute basic and diluted loss per common share (in thousands)	61,458	58,986	51,205

See accompanying notes to consolidated financial statements.

# STRESSGEN BIOTECHNOLOGIES CORPORATION

## CONSOLIDATED STATEMENT OF CASH FLOWS

(Canadian dollars in thousands)

	Years ended December 31,		
	2003	2002	2001
Cash flows from operating activities:			
Net loss	\$ (16,245)	\$ (28,802)	\$ (35,939)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	715	797	621
Compensation expense related to stock option grants	207	224	177
Unrealized foreign exchange loss (gain)	1,054	(20)	(1,462)
Loss (gain) on market value of investments	406	(145)	-
Changes in operating assets and liabilities	(2,652)	1,423	143
Net cash used in operating activities	<u>(16,515)</u>	<u>(26,523)</u>	<u>(36,460)</u>
Cash flows from investing activities:			
Purchase of short-term investments	(33,255)	(76,641)	(37,095)
Sales and maturities of short-term investments	15,025	91,388	78,346
Purchase of plant and equipment	(165)	(380)	(1,783)
Net cash (used in) provided by investing activities	<u>(18,395)</u>	<u>14,367</u>	<u>39,468</u>
Cash flows from financing activities:			
Proceeds from issuance of common shares	23,672	10,604	29,248
Proceeds from borrowings	1,004	-	102
Repayment of borrowings	(459)	(535)	(454)
Net cash provided by financing activities	<u>24,217</u>	<u>10,069</u>	<u>28,896</u>
Effect of exchange rate changes on cash and cash equivalents	<u>(513)</u>	<u>(49)</u>	<u>921</u>
Increase (decrease) in cash and cash equivalents	(11,206)	(2,136)	32,825
Cash and cash equivalents, beginning of year	31,202	33,338	513
Cash and cash equivalents, end of year	<u>\$ 19,996</u>	<u>\$ 31,202</u>	<u>\$ 33,338</u>

See accompanying notes to consolidated financial statements.

**STRESSGEN BIOTECHNOLOGIES CORPORATION**  
**CONSOLIDATED STATEMENT OF STOCKHOLDERS' EQUITY**  
(Canadian dollars in thousands, except share data)

	Common shares and other equity		Warrants		Def Stock Comp	Accumulated Deficit	Total
	Number	Amount	Number	Amount			
Balance at January 1, 2001	49,892,271	\$ 134,739	3,833,500	\$ -	\$ -	\$ (69,308)	\$ 65,431
Issued for cash on exercise of stock options	423,219	973	-	-	-	-	973
Issued for cash on exercise of Warrants	577,298	2,119	(577,298)	-	-	-	2,119
Issued for cash, net of issue costs	6,699,100	26,156	-	-	-	-	26,156
Deferred stock compensation	-	807	-	-	(807)	-	-
Compensation expense related to stock option grants	-	-	-	-	177	-	177
Net loss	-	-	-	-	-	(35,939)	(35,939)
Balance at December 31, 2001	57,591,888	164,794	3,256,202	-	(630)	(105,247)	58,917
Issued for cash on exercise of stock options	575,902	1,706	-	-	-	-	1,706
Conversion of warrants to common shares	3,963	-	(25,057)	-	-	-	-
Warrants issued in connection with Roche Collaboration	-	-	2,036,435	1,264	-	-	1,264
Issued for cash in connection with Roche Collaboration	2,036,436	7,657	-	-	-	-	7,657
Other, net	1,800	(37)	-	-	28	-	(9)
Compensation expense related to stock option grants	-	-	-	-	210	-	210
Net loss	-	-	-	-	-	(28,802)	(28,802)
Balance at December 31, 2002	60,209,989	174,120	5,267,580	1,264	(392)	(134,049)	40,943
Issued for cash on exercise of stock options	229,516	375	-	-	-	-	375
Issued for cash, net of issue costs	10,638,298	17,796	5,319,149	904	-	-	18,700
Adjustment due to price difference in warrant transaction related to Roche Collaboration	-	-	191,739	-	-	-	-
Conversion of warrants to common shares in connection with Roche Collaboration	1,413,600	5,352	(1,413,600)	(758)	-	-	4,594
Expiration of warrants	-	-	(3,231,145)	-	-	-	-
Other, net	-	3	-	-	4	-	7
Compensation expense related to stock option grants	-	-	-	-	203	-	203
Net loss	-	-	-	-	-	(16,245)	(16,245)
Balance at December 31, 2003	72,491,403	\$ 197,646	6,133,723	\$ 1,410	\$ (185)	\$ (150,294)	\$ 48,577

**Stressgen Biotechnologies Corporation**  
**Notes to Consolidated Financial Statements**  
(Canadian dollars)

**1. ORGANIZATION AND SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES**

Stressgen Biotechnologies Corporation (with its subsidiaries, "Stressgen" or the "Company") is a biopharmaceutical company focused on the development and commercialization of innovative stress protein-based immunotherapeutics. The Company is developing a broad range of products for the treatment of viral infections and related cancers. Its lead product is HspE7, which targets a broad spectrum of human papillomavirus ("HPV") related diseases. The Company has also initiated research studies to evaluate stress protein (also known as heat shock protein) fusions, made through its proprietary CoVal<sup>TM</sup> technology, for the treatment of hepatitis B and herpes simplex and is targeting hepatitis C. Further, Stressgen has an internationally recognized research product supply business with sales to scientists worldwide for the study of cellular stress, apoptosis, oxidative stress and neurobiology.

*Basis of presentation*

The consolidated financial statements include the assets, liabilities and operating results of the Company and its wholly-owned subsidiaries. Intercompany accounts and transactions have been eliminated in consolidation. Certain prior year balances have been reclassified to conform to current year presentation.

*Financial statements and estimates*

The financial statements, in the opinion of management, include all adjustments necessary for their fair presentation in conformity with Canadian generally accepted accounting principles ("Canadian GAAP"), and conform in all material respects with accounting principles generally accepted in the United States of America ("U.S. GAAP"), except as discussed in Note 11.

The preparation of financial statements in conformity with generally accepted accounting principles requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenue and expenses and related disclosures as of the date of the financial statements. Significant estimates are used for, but not limited to, reporting revenue recognition, clinical trial costs, stock based compensation and the allocation of indirect costs. Actual results could differ from such estimates.

*Foreign currency translation*

The Company and its subsidiaries use the Canadian dollar as their functional currency. Monetary assets and liabilities that are denominated in U.S. dollars are translated into Canadian dollars at the rate of exchange prevailing at the balance sheet date. Non-monetary assets and liabilities are translated at historical rates. Revenues and expenses are translated at the average rate of exchange for the period of such transactions.

**Stressgen Biotechnologies Corporation**  
**Notes to Consolidated Financial Statements**  
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**1. ORGANIZATION AND SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES (continued)**

*Revenue recognition*

Revenue from product sales is recognized upon delivery to customers when persuasive evidence of an arrangement exists, the price is fixed or determinable and collection is reasonably assured. Revenue also includes amounts charged for shipping and handling costs.

Revenue from collaborative research and development ("R&D") arrangements may include multiple elements within a single contract. The Company's accounting policy complies with the revenue determination requirements set forth in EITF 00-21, *Accounting for Revenue Arrangements with Multiple Deliverables*, and EIC 142, *Revenue Arrangements with Multiple Deliverables*, relating to the separation of multiple deliverables into individual accounting units with determinable fair values. Payments received under collaborative arrangements may include the following: non-refundable fees at inception of contract for technology rights; funding for services performed; milestone payments for specific achievements; and payments based upon resulting sales of products.

The Company recognizes collaborative research and development revenues as services are rendered consistent with the performance requirements of the contract. Revenue from non-refundable contract fees where the Company has continuing involvement through research and development collaborations or other contractual obligations, less the fair market value of any related warrants, is recognized ratably over the development period or the period for which Stressgen continues to have a performance obligation. The period of development is evaluated on a regular basis. During December 2003, the Company increased the development period to reflect management's research and development plan. Revenue from performance milestones is recognized upon the achievement of the milestones as specified in the agreement, provided payment is proportionate to the effort expended. Payments are recorded as deferred revenue if they are received in advance of performance or delivery.

*Clinical trial accruals*

The Company recognizes expenses related to its ongoing clinical trials using a methodology designed to accrue estimated costs in the appropriate accounting periods. The Company recognizes clinical trial costs in three distinct phases: the start-up phase, the patient accrual phase, and the close-out phase. The total estimated trial cost is divided into these three phases based on the tasks involved in conducting the trial. Based on the design of the trial, the cost of each phase could vary from trial to trial. Upon the start of the trial, the start-up portion of the trial contract is accrued. As patients enter the trial, the patient accrual cost is ratably recognized. Once the study is complete and analysis of the

**Stressgen Biotechnologies Corporation**  
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**1. ORGANIZATION AND SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES (continued)**

patient data has been initiated, the close-out portion of the trial is recognized.

*Stock-based compensation plan*

Multiple standards exist regarding the recognition, measurement and disclosure of stock-based compensation and other stock-based payments. The Company has adopted the recommendations of the CICA Handbook section 3870, *Stock-Based Compensation and Other Stock-Based Payments*, effective January 1, 2002. This standard requires that all stock-based awards made to non-employees be measured and recognized using a fair value based method. The standard encourages the use of a fair value based method for all awards granted to employees, but requires the use of a fair value based method only for direct awards of stock, stock appreciation rights, and awards that call for settlement in cash or other assets. Awards that a company has the ability to settle in stock are recorded as equity, whereas awards that the entity is required to or has a practice of settling in cash are recorded as liabilities.

The Company's accounting methods for stock-based compensation plans also materially follow the guidance under the recognition and measurement principles of APB Opinion No. 25, *Accounting for Stock Issued to Employees*, and related interpretations. The Company has two stock-based compensation plans, which are described in Note 5. New option grants are made with an exercise price equal to the fair market value of the underlying common stock. No compensation expense is recognized for options granted at fair market value under the plan when stock options are issued to directors and employees. Deferred stock compensation charges arise where stock options are granted at exercise prices less than the fair value of the underlying stock and are amortized to expense over the vesting period of the option. Any consideration paid by directors, employees and others on exercise of stock options is credited to share capital.

The following table summarizes the effect on net loss and loss per share if the Company had applied the fair value recognition provisions of the Financial Accounting Standards Board ("FASB") Statement No. 123, *Accounting for Stock-Based Compensation*, to stock-based employee compensation.

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**1. ORGANIZATION AND SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES (continued)**

(In thousands, except per share amounts)

	<u>Years ended December 31,</u>		
	<u>2003</u>	<u>2002</u>	<u>2001</u>
Net loss under Canadian GAAP	<u>\$ (16,245)</u>	<u>\$ (28,802)</u>	<u>\$ (35,939)</u>
Net loss under U.S. GAAP (See Note 11 for reconciliation to Canadian GAAP)	<u>\$ (15,298)</u>	<u>\$ (28,922)</u>	<u>\$ (36,341)</u>
Employee stock compensation expense included in net loss under Canadian GAAP	207	224	177
Employee stock compensation expense included in net loss under U.S. GAAP	207	224	258
Additional employee compensation expense under the fair value method	<u>(2,419)</u>	<u>(2,850)</u>	<u>(3,232)</u>
Pro forma net loss under Canadian GAAP	<u>\$ (18,457)</u>	<u>\$ (31,428)</u>	<u>\$ (38,994)</u>
Pro forma net loss under U.S. GAAP	<u>\$ (17,510)</u>	<u>\$ (31,548)</u>	<u>\$ (39,315)</u>
Pro forma basic loss per common share under Canadian GAAP	<u>\$ (0.30)</u>	<u>\$ (0.53)</u>	<u>\$ (0.76)</u>
Pro forma basic loss per common share under U.S. GAAP	<u>\$ (0.28)</u>	<u>\$ (0.53)</u>	<u>\$ (0.77)</u>

The weighted-average per-share fair values of the individual options granted during 2003, 2002 and 2001 were \$1.06, \$2.63 and \$2.50, respectively.

The fair values of the options were determined using a Black-Scholes option-pricing model with the following assumptions:

	<u>Years ended December 31,</u>		
	<u>2003</u>	<u>2002</u>	<u>2001</u>
Dividend yield	0%	0%	0%
Volatility	75%	78%	55%
Risk-free interest rate	2.54%	3.50%	3.57%
Expected life	4 years	4 years	4 years

*Cash, cash equivalents and short-term investments*

Cash and cash equivalents consist of cash and highly liquid investments, including investment grade corporate debt securities with original maturities when acquired of three months or less. Short-term investments consist of investment grade securities, which are capable of prompt liquidation and are carried at the lower of cost plus accrued interest or quoted market value.

**Stressgen Biotechnologies Corporation**  
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**1. ORGANIZATION AND SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES (continued)**

*Inventories*

Inventories are valued at the lower of average cost or net realizable value.

*Plant and equipment*

Plant and equipment are recorded at cost and depreciated over their estimated useful lives on a declining-balance basis, except for leasehold improvements, which are amortized on a straight-line basis over the lesser of the lease term or the estimated useful life. The approximate annual depreciation and amortization rates are as follows:

Laboratory equipment	20%
Computer equipment	30%
Furniture and equipment	20%
Leasehold improvements	the lesser of the lease term or the estimated useful life

*Impairment of long-lived assets*

The Company assesses potential impairment to its long-lived assets when there is evidence that events or changes in circumstances exist. The recoverability of long-lived assets is determined by evaluating whether the carrying value of such assets can be recovered from estimated undiscounted future operating cash flows. Should an impairment exist, the impairment loss would be measured based on the excess of the carrying value of the assets over the present value of the future operating cash flows. The Company has not identified any such impairment losses to date.

*Fair value of financial instruments*

Management believes that the carrying values of financial instruments, including cash and cash equivalents, short-term investments, accounts receivable, accounts payable, and accrued liabilities approximate fair value as a result of the short-term maturities of these instruments. The carrying value of fixed rate capital leases and term loan obligations approximate fair value, as the imputed interest rate is approximately equivalent to the market rates charged on similar arrangements.

*Concentration of credit risk*

The Company invests its excess cash principally in investment grade government and corporate debt securities. The Company has established guidelines relative to diversification and maturities that maintain safety and liquidity. These guidelines are periodically reviewed and modified to reflect changes in market conditions. The

**Stressgen Biotechnologies Corporation**  
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**1. ORGANIZATION AND SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES (continued)**

Company has not experienced any significant losses on its cash equivalents or short-term investments.

The Company extends credit on an uncollateralized basis primarily to its customers in the U.S. The Company has not experienced significant credit losses on customer's accounts. The Company has derived 100% of its collaboration revenue from Roche.

*Research and development costs*

Research and development costs associated with the Company's various research and development programs consist of direct and indirect expenditures, including a reasonable allocation of overhead expenses. Overhead expenses are comprised of general and administrative support provided to the research and development programs. These expenses include costs associated with support activities such as information technology, finance and human resources as well as for the use of facilities. Research and development costs are expensed as incurred, unless they meet generally accepted accounting criteria for deferral and amortization. The Company reassesses whether it has met the relevant criteria for deferral and amortization at each reporting date. To date, no research and development costs have been deferred.

*Income taxes*

Future income tax assets and liabilities relate to the expected future tax consequences of differences between the carrying amount of balance sheet items and their corresponding tax values, and for loss carry-forwards and other deductions. Future tax assets, if any, are recognized only to the extent that, in the opinion of management, it is more likely than not that the future income tax assets will be realized. Future income tax assets and liabilities are adjusted for the effects of changes in tax laws and rates on the date of enactment or substantive enactment.

*Net loss per share*

Net loss per share is computed using the weighted average number of common shares outstanding. Basic and diluted net loss per common share amounts are equivalent for the periods presented as the inclusion of common stock equivalents (options and warrants) in the number of shares used for the diluted computation would be anti-dilutive.

*New Accounting Pronouncements*

In September 2003, the AcSB released revised transitional provisions for Stock-Based Compensation and Other Stock-Based Payments, Section 3870, to provide the same

# Stressgen Biotechnologies Corporation

## Notes to Consolidated Financial Statements

(Canadian dollars)

### 1. ORGANIZATION AND SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES (continued)

alternative methods of transition as is provided in the US for voluntary adoption of the fair value based method of accounting. These provisions permit either retroactive (with or without restatement) or prospective application of the recognition provisions to awards not previously accounted for at fair value. Prospective application is only available to enterprises that elect to apply the fair value based method of accounting to that type of award for fiscal years beginning before January 1, 2004.

The AcSB has also amended Section 3870 to require that all transactions whereby goods and services are received in exchange for stock-based compensation and other payments result in expenses that should be recognized in financial statements, and that this requirement would be applicable for financial periods beginning on or after January 1, 2004. Section 3870 requires that share-based transactions should be measured on a fair value basis. The Company will adopt the provisions of AcSB Section 3870 beginning January 1, 2004.

The FASB issued SFAS No. 148, *Accounting for Stock-Based Compensation, Transition and Disclosure* in December 2002. SFAS No. 148 provides alternative transition methods for entities that voluntarily elect to adopt the fair value recognition provisions of FASB Statement No. 123, *Accounting for Stock-Based Compensation*, to stock-based employee compensation. In addition, SFAS No. 148 requires more prominent pro forma disclosures of the effect on net income and earnings per share if the company had applied these fair value recognition provisions. The transition and annual disclosure provisions of SFAS No. 148 are effective for fiscal years ending after December 15, 2002. While the Company has not elected to adopt the provisions in SFAS 123, pro forma financial results are discussed in Note 1.

### 2. COLLABORATIVE AGREEMENT

On December 2, 2003, the Company announced that it had restructured its June 24, 2002 collaboration agreement with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. (together, "Roche"), providing for the development and commercialization of Stressgen's pharmaceutical fusion product candidate, HspE7. The parties agreed to restructure the agreement to facilitate the clinical development by Stressgen of HspE7 in recurrent respiratory papillomatosis and additional indications caused by the human papillomavirus, while providing Roche an opportunity to purchase a license to develop a second generation HspE7 product targeting genital warts. Roche may pay a fee to obtain exclusive rights to the first generation HspE7 product. Assuming this fee is paid and all HspE7 development and commercial milestones are achieved and Roche exercises its rights to certain other CoVal<sup>TM</sup> fusion product candidates, payments to the Company, excluding sales-based payments (similar to royalties), could approximate \$340,500,000,

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**2. COLLABORATIVE AGREEMENT (continued)**

beyond the approximately \$32,250,000 received from Roche relating to the development of a first generation HspE7 product to date.

Under the terms of the restructured collaboration agreement, the extent of control that the Company originally retained for developing and marketing the first generation HspE7 product for RRP will expand to all indications other than genital warts. Stressgen will assume all responsibility for all manufacturing and other costs of the indications it chooses to develop. In addition Roche can obtain exclusive rights to the first generation HspE7 product by paying Stressgen a fee and event-driven milestones aggregating up to \$207,000,000. Until March 31, 2005 Stressgen can elect, under defined circumstances, to terminate Roche's exclusive rights to the first generation HspE7 product.

If Roche exercises its exclusive rights to the first generation HspE7 product, it will fund all prospective costs for the first generation product. Further, the Company can elect to launch a sales force in the U.S. and Canada and record sales for three years after regulatory approval in those countries, in which case we will pay Roche a mid single-digit percentage or a low double-digit percentage of net sales, depending upon the timing and occurrence of Roche's exercise. Under these conditions, no earlier than three years after market launch of HspE7, Roche can begin recording sales in the U.S. and Canada. Once Roche begins recording sales in those countries, the Company will receive sales-based payments, which are expected to approximate 35% of Roche's net HspE7 product sales. In the rest of the world, Roche will record sales immediately after market launch and the Company will receive sales-based payments of 20% of Roche's net sales.

For the years ended December 31, 2003 and 2002, the Company recognized collaborative R&D revenue of \$8,094,000 and \$8,370,000, respectively, relating to development activities in support of Roche's activities under the June 2002 collaboration agreement and amortization of up-front license fees in accordance with SAB No. 101 "Revenue Recognition in Financial Statements." Collaborative R&D revenue in 2003 includes \$4,912,000 for development activities, \$2,214,000 for a time based milestone payment and \$968,000 for the amortization of upfront license fees. Collaborative R&D revenue in 2002 includes \$7,815,000 for development activities and \$555,000 from the amortization of up-front license fees.

**3. BALANCE SHEET DETAILS**

At December 31, 2003 and 2002, our short-term investments consisted of corporate debt securities and government issued debt securities, which had a net book value and market value of \$32,094,000 and \$14,811,000, respectively.

The MIT/Whitehead license agreement discussed in Note 4 requires certain license maintenance fees and royalty payments. Upon receiving the upfront license fee payment

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**3. BALANCE SHEET DETAILS (continued)**

from Roche in 2002, the Company recorded a \$634,320 payable due to MIT/Whitehead and a related deferred expense. The payment was made in January 2003. The Company recognizes the related deferred expense over the development period, which was adjusted in conjunction with the restructured Roche collaborative agreement. At December 31, 2003 and 2002 the Company had a total of \$347,000 and \$561,778 of deferred expense related to this payment.

The Company recorded an additional \$221,000 payable due to MIT/Whitehead related to the \$2,214,000 milestone payment received from Roche in April 2003. The payment was made to MIT/Whitehead during the third quarter of 2003.

The following tables provide details of selected balance sheet items:

(In thousands)	December 31,			
	2003		2002	
	Cost	Accumulated Depreciation	Net Book Value	Net Book Value
Plant and equipment:				
Laboratory equipment	\$ 4,397	\$ 2,771	\$ 1,626	\$ 1,932
Computer equipment	1,025	733	292	393
Furniture and fixtures	563	391	172	240
Leasehold improvements	716	610	106	181
	\$ 6,701	\$ 4,505	\$ 2,196	\$ 2,746

**Stressgen Biotechnologies Corporation**  
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**3. BALANCE SHEET DETAILS (continued)**

(In thousands)	<u>December 31,</u>	
	<u>2003</u>	<u>2002</u>
Accounts receivable:		
Trade accounts receivable	\$ 492	\$ 527
Collaborative receivable	277	3,790
Less: allowance for doubtful accounts	<u>(36)</u>	<u>(38)</u>
	<u>\$ 733</u>	<u>\$ 4,279</u>
Inventories:		
Raw materials, net	\$ 202	\$ 417
Work in process, net	146	145
Finished goods, net	291	276
	<u>\$ 639</u>	<u>\$ 838</u>
Accounts payable and accrued liabilities:		
Trade accounts payable	\$ 1,461	\$ 3,607
Clinical trial accruals	1,409	3,133
Accrued compensation and benefits	1,009	1,274
Royalty payable	-	634
Other accrued liabilities	96	185
	<u>\$ 3,975</u>	<u>\$ 8,833</u>

**4. COMMITMENTS AND CONTINGENCIES**

*Leases*

The Company has entered into operating lease agreements for office and laboratory space that expire at various times through 2005. These leases require the Company to make minimum lease payments, plus a share of operating costs, taxes, insurance and maintenance.

At December 31, 2003 and 2002, \$1,125,000 and \$580,000, respectively, were used and outstanding in the form of fixed rate capital leases and term loan agreements. In September 2003 the Company entered into a 36-month term loan agreement with Oxford Finance Corporation, collateralized by equipment owned by the Company. At December 31, 2003 there was \$906,000 outstanding on the loan. Under the terms of the agreement, the Company must issue a letter of credit for the outstanding loan balance if combined cash, cash equivalents, and short-term investments fall below \$6,000,000.

At December 31, 2003 total future minimum lease commitments under operating leases; fixed rate capital leases and term loan agreements are as follows:

**Stressgen Biotechnologies Corporation**  
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**4. COMMITMENTS AND CONTINGENCIES (continued)**

(In thousands)

Year ending December 31,	<u>Operating</u>	<u>Capital</u>	<u>Term loan</u>	<u>Total Capital and term loan</u>
2004	\$ 875	\$ 176	\$ 440	\$ 616
2005	819	55	439	494
2006	-	-	161	161
Total	<u>\$ 1,694</u>	231	1,040	1,271
Less: amount representing interest				<u>(146)</u>
Present value of minimum payments				1,125
Less: current portion				<u>(518)</u>
Long term notes payable				<u>\$ 607</u>

*Patent License Agreement*

The Company has a worldwide, exclusive license agreement with Massachusetts Institute of Technology and the Whitehead Institute for Biomedical Research. The patents and patent applications covered by this license agreement include various pending applications and continuation-in-part applications and their foreign counterparts, including patent applications filed in the U.S., Canada and Japan in 1994 for the use of Hsp fusions with viral or cancer-associated antigens as immunotherapeutics. Historically, the Company's patent-related costs are related to therapeutic products that have not obtained regulatory approval and are not marketable. As a result, the Company has treated such costs as costs for which recoverability cannot be determined, and has expensed them as incurred.

**5. STOCKHOLDERS' EQUITY**

*Common Shares*

In June 2002 the Company issued 2,036,436 common shares for \$7,657,000 pursuant to the collaboration agreement with Roche (see Note 2). The equity was issued at a per share price determined by the weighted average price of common shares of the Company during the ten business days prior to the Roche transaction.

At the time of the original collaboration agreement, Roche received two warrants to purchase the common stock of Stressgen. The Company allocated \$1,264,000 as the fair value of the warrants, determined by an independent valuation expert. In April 2003 Roche exercised the first warrant to acquire 1,413,600 common shares at \$3.25, resulting in net proceeds of \$4,594,000 to the Company. Under the original collaboration agreement, the Company had the right to call the second warrant resulting in an issuance

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**5. STOCKHOLDERS' EQUITY (continued)**

of a range of shares and exercise price depending upon the price of the Company's common stock. In connection with the restructured collaboration agreement, Roche has a continued right, but not an obligation, to exercise the second warrant for 814,574 shares at a purchase price of \$3.76 per share at any time until June 28, 2007.

The Company has unlimited authorized common share capital.

*Common Share Financings*

In December 2003, the Company completed an offering of 10,638,298 units at a price of \$1.88 per Unit for gross proceeds of \$20,000,000. Each unit consists of one common share in the capital of the Company and one-half of one common share purchase warrant. The Company incurred total share issue costs on the offering of approximately \$1,300,000. Under the conditions of the offering, the Company agreed to indemnify the underwriters and their broker/dealer affiliates against certain liabilities, including liabilities under the United States securities laws and under Canadian securities legislation and to contribute to payments that the underwriters may be required to make in respect thereof.

In 2001, the Company completed an offering for 6,699,100 common shares at \$4.15 per share for gross proceeds of \$27,801,000. The Company incurred total share issue costs on the offering of \$1,645,000.

Stockholders' equity at December 31, 2003 and 2002 includes \$2,207,000 and \$2,179,000, respectively, of contributed surplus.

*1998 Special Warrants*

In 1998 the Company issued Class B Warrants to purchase 4,000,000 shares for \$3.30 per share or pursuant to a cashless exercise provision. The unexercised Class B Warrants expired on June 12, 2003. As a result the Company no longer has the obligation to issue up to 3,231,145 common shares that had been reserved for issuance upon exercise of the Class B Warrants.

*Employee Share Option Plans*

In 2001, the Company issued out-of-plan stock options prior to stockholder approval of the 2001 Equity Incentive Plan (the "2001 Plan"). Between the date of grant and stockholder approval, the market price of the Company's common stock increased, resulting in deferred compensation of \$807,000 associated with these options. The deferred compensation has been amortized to expense over the vesting period of the granted options. At that time, the Company stopped granting options under its pre-

**Stressgen Biotechnologies Corporation**  
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**5. STOCKHOLDERS' EQUITY (Continued)**

existing 1996 Share Incentive Plan. At December 31, 2003, there were 4,978,118 total options issued and outstanding under the two plans, at exercise prices ranging from \$1.22 to \$8.00 per share with remaining weighted average contractual lives of 7 years to 9 years, and 358,986 options available for future grant under the 2001 Plan.

The following table summarizes stock option activity under the Plans:

	Number of Shares	Weighted Average Exercise Price
Balance at January 1, 2001	3,374,177	\$ 4.05
Granted	1,415,000	5.24
Exercised	(423,219)	2.30
Cancelled	(190,375)	4.92
Balance at December 31, 2001	4,175,583	4.59
Granted	1,092,250	4.41
Exercised	(575,902)	2.96
Cancelled	(387,368)	5.46
Balance at December 31, 2002	4,304,563	4.69
Granted	1,157,500	1.80
Exercised	(229,516)	1.63
Cancelled	(254,429)	3.66
Balance at December 31, 2003	<u>4,978,118</u>	\$ 4.21

The following table summarizes information related to all stock options outstanding and exercisable at December 31, 2003:

Range of Exercise Prices	Options Outstanding			Options Exercisable		
	Number Outstanding	Weighted Average Remaining Contractual Life (in years)	Weighted Average Exercise Price	Number Exercisable	Weighted Average Exercise Price	
\$1.22 - \$1.99	1,353,453	8.1	\$ 1.71	750,414	\$ 1.76	
\$2.00 - \$3.99	626,000	8.7	3.24	304,525	3.50	
\$4.00 - \$5.99	1,464,565	7.5	4.87	1,082,770	4.87	
\$6.00 - \$8.00	1,534,100	6.5	6.19	1,473,661	6.19	
	<u>4,978,118</u>			<u>3,611,370</u>		

**Stressgen Biotechnologies Corporation**  
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**6. INCOME TAXES**

The reported income tax recovery differs from the amount computed by applying the Canadian basic statutory rates to the net loss. The reasons for this difference and the related tax effects are as follows:

(In thousands)	Years ended December 31,		
	2003	2002	2001
Canadian basic statutory tax rates	35.6%	39.6%	45.0%
Expected income tax recovery	\$ (5,786)	\$ (11,411)	\$ (16,173)
Foreign tax rate differences	1,669	(2,080)	22,208
Prior year losses producing current benefit	-	(125)	(7,412)
Losses producing no current tax benefit	2,232	13,682	2,361
Non-deductible expenses and other deductions	21	(54)	94
Research and development expenses	2,143	900	(193)
Benefit of temporary differences (recognized) not recognized	(279)	(912)	(885)
	<u>\$ -</u>	<u>\$ -</u>	<u>\$ -</u>

Future income taxes result principally from temporary differences in the recognition of certain revenue and expense items for financial and income tax reporting purposes. Significant components of the Company's future tax assets and liabilities are as follows:

(In thousands)	December 31,	
	2003	2002
Future income tax assets:		
Tax loss carry-forwards	\$ 20,001	\$ 27,055
Tax credits	7,450	-
Research and development expenses	8,000	5,857
Book and tax base differences on assets and liabilities	1,192	1,472
Total future income tax assets	36,643	34,384
Valuation allowance for future income tax assets	(36,643)	(34,384)
Net future income tax assets	<u>\$ -</u>	<u>\$ -</u>
Future income tax liabilities:		
Book and tax base differences on assets and liabilities	\$ -	\$ -
Net future income tax liabilities	<u>\$ -</u>	<u>\$ -</u>

Due to the uncertainty surrounding the realization of the future income tax assets, the

**Stressgen Biotechnologies Corporation**  
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**6. INCOME TAXES (continued)**

Company has a 100% valuation allowance against its future income tax assets. The valuation allowance increased by \$2,259,000 during the year 2003.

At December 31, 2003, the Company has approximately \$22,460,000 of scientific research and experimental development expenditures available for unlimited carry forward, \$51,975,680 of non-capital losses expiring between 2006 and 2010 and \$7,450,000 of unclaimed tax credits expiring between 2004 and 2012, all of which may be used to reduce future Canadian income taxes otherwise payable. In addition, the Company has U.S. \$930,000 of net operating losses expiring between 2011 and 2023, which may be used to reduce future U.S. income taxes otherwise payable.

**7. RELATED PARTY TRANSACTIONS**

Until the annual meeting in 2002 an independent contractor who is a researcher in the area of heat shock proteins also served as a director of the Company. In 2002 and 2001, this individual received consulting fees of \$50,000. There were no related party transactions in 2003.

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**8. SEGMENT INFORMATION**

The Company manages its operations in two reportable segments, Biotechnology and Bioreagents. Revenues are allocated to the countries based on customer locations.

(In thousands)	<u>Years ended December 31,</u>		
	<u>2003</u>	<u>2002</u>	<u>2001</u>
<b>Biotechnology</b>			
Collaborative R&D revenue	\$ 8,094	\$ 8,370	\$ -
Operating expenses:			
Research and development	19,289	32,353	34,906
Selling, general and administrative	5,602	6,656	6,310
	<u>24,891</u>	<u>39,009</u>	<u>41,216</u>
Operating loss	<u>\$ (16,797)</u>	<u>\$ (30,639)</u>	<u>\$(41,216)</u>
<b>Bioreagents</b>			
Revenues:			
U.S.	\$ 3,461	\$ 3,733	\$ 3,514
Canada	213	272	276
Other	1,651	1,667	1,629
	<u>5,325</u>	<u>5,672</u>	<u>5,419</u>
Operating expenses:			
Research and development	1,576	1,322	1,000
Selling, general and administrative	1,701	1,753	1,472
Cost of bioreagent sales	1,312	1,635	1,573
	<u>4,589</u>	<u>4,710</u>	<u>4,045</u>
Operating income	<u>\$ 736</u>	<u>\$ 962</u>	<u>\$ 1,374</u>
<b>Totals</b>			
Revenue:			
Collaborative R&D revenue	\$ 8,094	\$ 8,370	\$ -
Bioreagent sales	5,325	5,672	5,419
Total revenue	<u>13,419</u>	<u>14,042</u>	<u>5,419</u>
Operating expenses:			
Research and development	20,865	33,675	35,906
Selling, general and administrative	7,303	8,409	7,782
Cost of bioreagent sales	1,312	1,635	1,573
	<u>29,480</u>	<u>43,719</u>	<u>45,261</u>
Operating loss	<u>\$ (16,061)</u>	<u>\$ (29,677)</u>	<u>\$(39,842)</u>

**Stressgen Biotechnologies Corporation**  
**Notes to Consolidated Financial Statements**  
(Canadian dollars)

**8. SEGMENT INFORMATION (Continued)**

The Company does not allocate interest and other income, and interest on capital lease obligations to each segment.

Long-lived assets are allocated geographically as follows:

(In thousands)	<u>December 31,</u>	
	<u>2003</u>	<u>2002</u>
Canada	\$ 1,953	\$ 2,432
US	243	314
	<u>\$ 2,196</u>	<u>\$ 2,746</u>

At December 31, 2003 \$2,006,000 of plant and equipment support the Biotechnology operating segment while the remaining \$190,000 support the Bioreagent operating segment.

**9. SUPPLEMENTAL CASH FLOW INFORMATION**

(In thousands)

The change in operating assets and liabilities:

	<u>December 31,</u>		
	<u>2003</u>	<u>2002</u>	<u>2001</u>
Collaborative receivable	\$ 3,513	\$ (3,790)	\$ -
Trade receivables	33	120	17
Inventories	199	77	(182)
Other current assets	6	(98)	(22)
Deferred expenses, net of current portion	161	(421)	-
Deferred revenue	(1,706)	4,459	-
Accounts payable and accrued liabilities	(4,858)	1,076	330
	<u>\$ (2,652)</u>	<u>\$ 1,423</u>	<u>\$ 143</u>

(In thousands)

Supplemental disclosures of cash flows:

Interest paid

<u>Years ended December 31,</u>		
<u>2003</u>	<u>2002</u>	<u>2001</u>
<u>\$53</u>	<u>\$69</u>	<u>\$106</u>

Supplemental disclosures of non-cash investing and financing transactions:

Reversal of deferred compensation related to terminated employees  
Deferred stock compensation

\$4	\$28	\$ -
-	-	807

**Stressgen Biotechnologies Corporation**  
**Notes to Consolidated Financial Statements**  
(Canadian dollars)

**10. INTERIM FINANCIAL INFORMATION (UNAUDITED)**

The following is a summary of the unaudited quarterly results of operations for the years ended December 31, 2003 and 2002.

(In thousands except per share amounts)

	Quarter ended			
	March 31	June 30	September 30	December 31
<b>2003</b>				
Net revenues				
Canadian and U.S. GAAP	\$ 6,640	\$ 2,881	\$ 2,171	\$ 1,727
Research and development expenses				
Canadian and U.S. GAAP	6,493	4,791	6,009	3,572
Net loss				
Canadian GAAP	(2,457)	(4,403)	(5,623)	(3,762)
U.S. GAAP	(2,248)	(4,222)	(5,463)	(3,365)
Basic loss per common share				
Canadian GAAP	\$ (0.04)	\$ (0.07)	\$ (0.09)	\$ (0.06)
U.S. GAAP	\$ (0.04)	\$ (0.07)	\$ (0.09)	\$ (0.05)
<b>2002</b>				
Net revenues				
Canadian and U.S. GAAP	\$ 1,405	\$ 1,491	\$ 5,826	\$ 5,320
Research and development expenses				
Canadian and U.S. GAAP	9,283	9,778	7,447	7,167
Net loss				
Canadian GAAP	(10,480)	(11,983)	(2,280)	(4,059)
U.S. GAAP	(10,044)	(11,229)	(3,668)	(3,981)
Basic loss per common share				
Canadian GAAP	\$ (0.18)	\$ (0.21)	\$ (0.04)	\$ (0.07)
U.S. GAAP	\$ (0.17)	\$ (0.19)	\$ (0.06)	\$ (0.07)

**Stressgen Biotechnologies Corporation**  
**Notes to Consolidated Financial Statements**  
(Canadian dollars)

**11. THE EFFECT OF APPLYING ACCOUNTING PRINCIPLES GENERALLY ACCEPTED IN THE U.S.**

These financial statements have been prepared in accordance with Canadian GAAP which, except as set out below, conform, in all material respects, to U.S. GAAP.

Effect on the consolidated financial statements:

*Balance Sheet*

(In thousands)

	<b>December 31,</b>	
	<b>2003</b>	<b>2002</b>
Current assets under Canadian GAAP	\$ 53,974	\$ 51,648
Adjustment to carrying value of short-term investments classified as available-for-sale securities (a)	-	-
Current assets under U.S. GAAP	\$ 53,974	\$ 51,648
Stockholders' equity under Canadian GAAP	\$ 48,577	\$ 40,943
Unrealized holding gains on available-for-sale securities (a)	-	-
Stockholders' equity under U.S. GAAP	\$ 48,577	\$ 40,943

**Stressgen Biotechnologies Corporation**  
**Notes to Consolidated Financial Statements**  
(Canadian dollars)

**11. THE EFFECT OF APPLYING ACCOUNTING PRINCIPLES GENERALLY  
ACCEPTED IN THE U.S. (Continued)**

*Statement of Operations*

(In thousands, except per share amounts)

	<u>Years ended December 31,</u>		
	<u>2003</u>	<u>2002</u>	<u>2001</u>
Net loss under Canadian GAAP	\$ (16,245)	\$ (28,802)	\$ (35,939)
Reversal of unrealized foreign exchange (gain) loss on available-for-sale securities (a)	541	(69)	(541)
Reversal of previous adjustment to short-term investments (a)	406	(51)	220
Stock-based compensation expense on stock options (b)	-	-	(81)
Net loss under U.S. GAAP	<u>\$ (15,298)</u>	<u>\$ (28,922)</u>	<u>\$ (36,341)</u>
Basic loss per common share under Canadian GAAP	<u>\$ (0.26)</u>	<u>\$ (0.49)</u>	<u>\$ (0.70)</u>
Basic loss per common share under U.S. GAAP	<u>\$ (0.25)</u>	<u>\$ (0.49)</u>	<u>\$ (0.71)</u>
Common shares used to compute basic loss per share under Canadian and U.S. GAAP	<u>61,458</u>	<u>58,986</u>	<u>51,205</u>

**Stressgen Biotechnologies Corporation**  
**Notes to Consolidated Financial Statements**  
(Canadian dollars)

**11. THE EFFECT OF APPLYING ACCOUNTING PRINCIPLES GENERALLY ACCEPTED IN THE U.S. (Continued)**

*Statement of Cash Flows*

(In thousands)

	Years ended December 31,		
	2003	2002	2001
Net cash used in operating activities under Canadian and U.S. GAAP	<u>\$ (16,515)</u>	<u>\$ (26,523)</u>	<u>\$ (36,460)</u>
Net cash (used in) provided by investing activities under Canadian and U.S. GAAP	<u>\$ (18,395)</u>	<u>\$ 14,367</u>	<u>\$ 39,468</u>
Net cash provided by financing activities under Canadian and U.S. GAAP	<u>\$ 24,217</u>	<u>\$ 10,069</u>	<u>\$ 28,896</u>

*Differences*

- (a) Under U.S. GAAP, Statement of Financial Accounting Standards ("SFAS") No. 115, *Accounting for Certain Investments in Debt and Equity Securities*, the Company has classified certain of its short-term securities as available-for-sale and, accordingly, has included the changes in net unrealized holding gains or losses on these securities in other comprehensive income rather than in operations.

SFAS No. 130, *Reporting Comprehensive Income* establishes standards for the reporting and display of comprehensive income and its components (revenue, expenses, gains and losses) in a full set of general-purpose financial statements.

**Stressgen Biotechnologies Corporation**  
**Notes to Consolidated Financial Statements**  
(Canadian dollars)

**11. THE EFFECT OF APPLYING ACCOUNTING PRINCIPLES GENERALLY ACCEPTED IN THE U.S. (Continued)**

*Differences (continued)*

(In thousands, except per share amounts)	Years ended December 31,		
	2003	2002	2001
Net loss under U.S. GAAP	\$ (15,298)	\$ (28,922)	\$ (36,341)
Other comprehensive income			
Adjustment to unrealized foreign exchange and market gains (losses) on available-for-sale investments	(947)	120	178
Comprehensive net loss under U.S. GAAP	\$ (16,245)	\$ (28,802)	\$ (36,163)
Comprehensive loss per share under U.S. GAAP	\$ (0.26)	\$ (0.49)	\$ (0.71)

(b) As permitted by SFAS No. 123, *Accounting for Stock-Based Compensation*, the Company has elected to follow APB Opinion No. 25, *Accounting for Stock Issued to Employees*, and related interpretations in accounting for its stock options. Under APB Opinion No. 25, if the exercise price of the Company's employee stock options equals or exceeds the fair market value of the underlying stock on the date of grant, no compensation expense is recognized. When the exercise price of the employee stock options is less than the fair value of the underlying stock on the date of grant, the Company records deferred stock compensation for the difference and amortizes this amount to expense over the vesting period of the options. Options or stock awards issued to non-employees are recorded at their fair value as determined in accordance with SFAS No. 123 and Emerging Issues Task Force ("EITF") 96-18, and recognized over the related service period. In March 2000, the Financial Accounting Standards Board ("FASB") issued Interpretation No. 44 (FIN No. 44), *Accounting for Certain Transactions Involving Stock Compensation - an interpretation of APB 25*. The compensation expense of \$81,000 in 2001 results from former employees becoming independent contractors and from option grants to non-employees. In 2003 and 2002 compensation expense was included in net income under Canadian GAAP.

See Note 1 for additional pro forma information related to stock compensation using the fair value method.

(\*) In accordance with the provisions of Accounting Principle Board ("APB") Opinion No. 25 for recording the value of contingently issuable (escrow) shares, the Company has recorded compensation expense on the release of these shares

**Stressgen Biotechnologies Corporation**  
**Notes to Consolidated Financial Statements**  
(Canadian dollars)

**11. THE EFFECT OF APPLYING ACCOUNTING PRINCIPLES GENERALLY  
ACCEPTED IN THE U.S. (Continued)**

*Differences (continued)*

based upon the excess of the market value over cost of the common shares on the dates that release was assured over their paid up amount. At December 31, 2003 there were no common shares held in escrow.

- (\*\*) SFAS No. 109, *Accounting for Income Taxes*, requires the Company to calculate its future income taxes using only enacted tax rates. This differs from Canadian GAAP, which uses substantially enacted tax rates. Since any change in the carrying value of the Company's future income tax assets would be offset by a 100% valuation allowance, there would be no effect on the Company's financial position or results of operations.

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

None.

**Item 9A. CONTROLS AND PROCEDURES**

We have carried out an evaluation, under the supervision and with the participation of management, including our President and Chief Executive Officer and our Vice President, Corporate Development and Chief Financial Officer, of the effectiveness of the design and operation of the Company's disclosure controls and procedures, as defined in the Securities Exchange Act of 1934 as amended, as of December 31, 2003. Based upon that evaluation, our President and Chief Executive Officer and our Vice President, Corporate Development and Chief Financial Officer concluded that our disclosure controls and procedures are effective in enabling us to record, process, summarize and report information required to be included in our periodic SEC filings within the required time period. There have been no significant changes in our internal controls or in other factors that could significantly affect internal controls subsequent to the date we carried out this evaluation.

**PART III**

**Item 10. OUR DIRECTORS, EXECUTIVE OFFICERS AND KEY EMPLOYEES**

Certain information about our directors and executive officers, the positions held by them and their ages as of February 12, 2004 are as follows:

<u>Name</u>	<u>Age</u>	<u>Position</u>
Joann Data, M.D., Ph.D. (1, 2)	59	Director
Kenneth Galbraith (3)	41	Director
Elizabeth M. Greetham (3)	54	Director
Ian Lennox (1, 3)	50	Director
Margot Northey, Ph. D. (2)	64	Director
Jay M. Short, Ph.D. (1)	45	Director
Daniel L. Kopolinski	61	Director, President and Chief Executive Officer
Howard T. Holden, Ph.D.	59	Vice President, Regulatory Affairs and Compliance
Gregory M. McKee	40	Vice President, Corporate Development and Chief Financial Officer
John R. Neefe, M.D.	60	Senior Vice President, Clinical Research
Marvin I. Siegel, Ph.D.	57	Executive Vice President, Research and Development

(1) Member of the Compensation Committee

(2) Member of the Governance Committee

(3) Member of the Audit Committee

**JOANN L. DATA, M.D., PH.D.** joined the Stressgen board of directors effective October 1, 2001. She has served at Amylin Pharmaceuticals, Inc. as Senior Vice President of Regulatory Affairs and Quality Assurance since August 1999. While at Amylin, she provided regulatory and clinical consulting services to Cortex Pharmaceuticals, Inc. in 2002 and 2003 and to Allergan Pharmaceuticals in 2003. Dr. Data previously served as Executive Vice President, Product Development and Regulatory Affairs for CoCensys. Her prior experience includes several positions at the Upjohn Company, including Corporate Vice President for Pharmaceutical Regulatory Affairs and Project Management, and a number of positions at Hoffmann-La Roche, including Vice President of Clinical Research and Development. Dr. Data has been an adjunct assistant professor in medicine and pharmacology at Duke University Medical Center since 1982 and at Cornell Medical Center since 1986. She earned her M.D. from Washington University School of Medicine and her Ph.D. in Pharmacology from Vanderbilt University.

**KENNETH GALBRAITH** has served as one of our directors since May 2000. Mr. Galbraith has been the President of Gigha Consulting Ltd., a technology consulting and investment management company, since October 2000. Mr. Galbraith has served as a director of several private and public biotechnology companies, including Micrologix Biotech Inc. since March 2001, Angiotech Pharmaceuticals since March 2000, Cardiome Pharma Inc. since May 2003 and Neuro Discovery Inc. since November 2001. From February 1988 to October 2000 he was employed by QLT Inc., a biotechnology company, where he progressed to the position of Executive Vice President and Chief Financial Officer. Mr. Galbraith was a founding Director and Chairman of the B.C. Biotechnology Alliance and a former Chair of one of Canada's Centres of Excellence Networks, the Canadian Bacterial Diseases Network. He is also a director of the Michael Smith Foundation for Health Research and the Fraser Health Authority. Mr. Galbraith received his B.Com. (Honours) degree from the University of British Columbia in 1985 and was admitted in British Columbia as a Chartered Accountant in 1988.

**ELIZABETH M. GREETHAM** has served as a Stressgen director since September 2002. Since December 2003 she has been the Chief Executive Officer and President of ACCL Financial Consultants. From August 2000 to October 2003 she served as the Chief Executive Officer and Chairman of the Board of DrugAbuse Sciences, Inc., a private biopharmaceutical company in Hayward, California. From March 1999 to October 2003 she worked at the same entity as Chief Financial Officer and Senior Vice President, Business Development. Before joining DrugAbuse Sciences, Ms. Greetham spent nearly a decade as a portfolio manager for Weiss, Peck & Greer, an institutional investment management firm. She managed the WPG Life Sciences Funds, L.P., which invests in select biotechnology stocks. She has over 25 years of investment experience as a portfolio manager and healthcare analyst in the U.S. and Europe. Ms. Greetham also serves as a member of the Board of Directors of publicly traded Guilford Pharmaceuticals and King Pharmaceuticals, Inc. Her prior board experience includes service on the boards of directors of Sangstat Medical Corporation, PathoGenesis Corporation and CliniChem Development Inc. Ms. Greetham earned a BSc and a MA (Hons.) from the University of Edinburgh, Scotland.

**R. IAN LENNOX** has served as one of our directors since May 2002. He is President and Chief Executive Officer of Pharmaceutical & Biotechnology Markets, MDS Inc., where he has served since April 2000. Prior to joining MDS Inc., Mr. Lennox was President and Chief Executive Officer of Phoenix International Life Sciences from 1999 to 2000; and President and Chief Executive Officer of Drug Royalty Corporation Inc. from 1997 to 1999. Mr. Lennox also held

many positions with Monsanto Company beginning in 1978, including President and Chief Executive Officer of Monsanto Company (Canada) Inc. from 1991-1997. Mr. Lennox currently serves on the board of directors and audit committee of KBSH Capital Management Inc. and as the Chairman of the Board and on the audit committee of MDS Proteomics. In the past he served on various boards of directors, including as the Chairman of the Boards of Drug Royalty Corporation Inc. and the Mississauga Hospital Foundation, and as director of Hemosol Inc., GenSci Regeneration Sciences Inc., Marsulex Inc. and the Mississauga Hospital. Mr. Lennox attended the Columbia University School of Business and received his Masters of Business and HSBc. in Physiology and Pharmacology from the University of Western Ontario.

**MARGOT NORTHEY, M.A., PH.D.** joined the Stressgen board of directors in June 2002. Dr. Northey was a professor and the dean of Queen's School of Business, Queen's University in Kingston, Ontario, from September 1995 to June 2002. She is also the author of several best-selling books on communications. Dr. Northey currently serves on diverse corporate boards, including the boards of public companies Aliant Inc., Nexfor Inc. and Alliance Atlantis, and privately held British Columbia Transmission Corp. and Wawanesa Insurance. She is a graduate of University of Toronto, with a M.A. and Ph.D. from York University.

**JAY M. SHORT, PH.D.** has served as one of our directors since March 1994. Dr. Short has been President, Chief Executive Officer, Chief Technology Officer, and a director for Diversa Corporation, a biotechnology company, since September 1994. Since February 1995 Dr. Short has also served as a director for Invitrogen Corporation, a biotechnology company. He previously served at biotechnology companies Stratacyte, Inc., as President and Strategene Cloning Systems from September 1985 to September 1994 as Vice President of Research and Development and Operations. Dr. Short received a Ph.D. in biochemistry from Case Western Reserve University and his B.A. in chemistry from Taylor University.

**DANIEL L. KORPOLINSKI** has served as our President and Chief Executive Officer, U.S. Operations, since March 2000, and as one of our directors and our President and Chief Executive Officer since May 2000. Mr. Korpilinski was President and CEO of Copley Pharmaceutical Inc., a generic pharmaceutical company, from September 1998 until the company was acquired by Teva Pharmaceutical Industries Ltd. in September 1999. He was also a director of Copley from August 1998 until its acquisition. Mr. Korpilinski served as President and Chief Executive Officer of Prodromics On Line, a software company, from June 1997 until August 1998. Between 1991 and 1996 Mr. Korpilinski served as the President and Chief Executive Officer of CoCensys Inc., a biotechnology company specializing in the development of therapeutics for the central nervous system. From 1988 to 1991, Mr. Korpilinski was President of Adria Laboratories North America, an oncology company. Mr. Korpilinski started his career in the pharmaceutical industry with the Upjohn Company, where he spent 24 years, ultimately in the capacity as an Executive Director of several pharmaceutical business groups. He received his B.S. from Niagra University in New York.

**HOWARD T. HOLDEN, PH.D.** has served as Vice President, Regulatory Affairs and Compliance since July 1, 2002. He served as Vice President, Regulatory Affairs and Compliance with Ligand Pharmaceuticals from September 1992 until he joined Stressgen. Prior to his employment with Ligand, Dr. Holden was Senior Director, Worldwide Regulatory Affairs at Parke-Davis Pharmaceutical Research Division of the Warner-Lambert Company (now Pfizer,

Inc.). Dr. Holden also spent 14 years at the National Cancer Institute as Section Head/Senior Investigator in the Cancer Therapy Evaluation Program and the Biological Response Modifiers Program. He received a Ph.D. in microbiology from the University of Miami and a B.A. in zoology from Drew University.

**GREGORY M. McKEE** has served as our Vice President, Corporate Development and Chief Financial Officer since January 15, 2004. From June 2003 to mid-January, 2004, he was our Vice President, Corporate Development and Strategic Planning. From July 2000 through June 2003 Mr. McKee served as Senior Director, Corporate Development for Valentis, Inc., a San Francisco based gene therapy company. Prior to his employment with Valentis, from June 1996 through December 1999, Mr. McKee served in several management positions at Genzyme Corporation, a biotechnology company. Mr. McKee also spent 5 years in investment banking. Mr. McKee earned an MBA from The Wharton School, a Masters of Arts in International Studies from The Joseph H. Lauder Institute at the University of Pennsylvania and graduated with a Bachelor of Arts degree in Economics from the University of Washington.

**JOHN R. NEEFE, M.D.** became our Senior Vice President Clinical Research in mid-2002, after serving as our Vice-President, Clinical Research and Regulatory Affairs starting in December 1998. Prior to joining Stressgen in 1998 Dr. Neefe served as Vice President, Clinical Oncology and International Director of Clinical Oncology at Sanofi Research Division, Sanofi Pharmaceuticals from mid-1995 to December 1998. From 1993 until its acquisition by Sanofi in 1995, Dr. Neefe was Senior Director of Sterling-Winthrop, leading the company's clinical oncology drug development unit. Dr. Neefe has also held a position as director of Clinical Research at Centocor, has attained academic appointments at the University of Kentucky and at Georgetown University and held a research position at the National Cancer Institute. Dr. Neefe received his B.A. from Harvard University and his M.D. from the University of Pennsylvania School of Medicine.

**MARVIN I. SIEGEL, PH.D.** has served as our Executive Vice President, Research & Development since March 1997. Dr. Siegel was a director of Delta Pharmaceuticals, Inc., a Chapel Hill, North Carolina pharmaceutical company between 1997 and 1999. From February 1995 to February 1997, Dr. Siegel was Vice President in charge of science and research and development, Terrapin Technologies Inc., a South San Francisco, California private company specializing in drugs for allergy, oncology and diabetes, which is now a public company known as Telik Inc. Dr. Siegel was a senior executive with Schering-Plough Research Institute in Kenilworth, N.J., from May 1982 to February 1994 where he was responsible for biological research in immunology and allergy. From August 1975 to May 1982 Dr. Siegel was a research scientist at Burroughs Wellcome Company in Research Triangle Park, NC. He has attained academic appointments at Rutgers University and at the School of Medicine of the University of North Carolina at Chapel Hill. Dr. Siegel received his B.S. from Lafayette College, his M.A. from Columbia University and his Ph.D. from The Johns Hopkins University School of Medicine in 1973. He is a Fellow of the American Academy of Asthma, Allergy and Immunology and of the American Institute of Chemists.

Each officer serves at the discretion of our Board of Directors. Our Articles permit the authorized number of directors to range from three to fifteen directors. We currently have seven directors and no vacancies.

## **Board Committees**

Our Board of Directors has established three standing committees, the Audit Committee, the Compensation Committee and our Governance Committee, which also acts as a nominating committee. Our Board of Directors has delegated certain responsibilities to each of these Committees and has also instructed each of them to perform certain advisory functions and make recommendations and report to our Board of Directors. Where considered prudent, certain matters falling under the responsibility of these Committees are at times dealt with at a meeting of the entire Board of Directors. Additional committees are established from time to time for particular purposes.

The Audit Committee meets with our financial management and the independent auditors to review and inquire into matters affecting financial reporting matters, the system of internal accounting and financial controls and procedures and audit procedures and plans. This Committee also makes recommendations to our Board of Directors regarding the appointment of independent auditors. In addition, the Audit Committee reviews and recommends for approval to our Board of Directors our annual financial statements, annual report and certain other documents regulatory authorities require. The Audit Committee is also responsible for approving the policies under which our financial management may invest the funds in excess of those required for current operations. In 2003, the Audit Committee met four times. The current members of the committee are Kenneth Galbraith, Elizabeth Greetham and Ian Lennox, none of whom is one of our current or former officers. The Board of Directors has determined that all three members of the Audit Committee are audit committee financial experts and are "unrelated directors" under Toronto Stock Exchange guidelines.

The Governance Committee is responsible for identifying, evaluating and recommending nominees for our Board of Directors and reviewing incumbent directors for re-election to our Board of Directors. Incumbent and potential new directors are evaluated by this Committee with the objective of obtaining a balanced mix of Board members with the experience and expertise to ensure that our Board of Directors is composed of individuals who will best serve our interests and assist management in reaching our strategic goals. The Governance Committee met once in 2003. The current members of the Governance Committee are Margot Northey and Joann Data. The Governance Committee will consider nominees for directors that are recommended by shareholders. Submissions should be directed to the Governance Committee in care of our corporate secretary and general counsel at the address set forth on the cover of this report.

The Compensation Committee is responsible for establishing and monitoring our long range plans and programs for attracting, training, developing and motivating employees. This Committee reviews recommendations for the appointment of persons to senior executive positions, considers terms of employment, including succession planning and matters of compensation and recommends any awards of over 20,000 shares to one individual under our 2001 Equity Incentive Plan. The Compensation Committee also reviews all compensation for executive officers reporting directly to the Chief Executive Officer, including the Named Executive Officers, for market comparability and reasonableness in light of the performance and realization of pre-established objectives of the executive officers. In 2003, this committee met three times. The current members of the committee are Joann Data, Ian Lennox and Jay Short.

## **Code of Ethics**

We have adopted a code of ethics that applies to all of our employees including the Named Executive Officers defined below. Copies of our current Code of Ethics may be requested from our corporate secretary and general counsel at the address set forth on the cover of this report for no charge.

## **Item 11. COMPENSATION OF DIRECTORS AND EXECUTIVE OFFICERS**

We hold annual elections for the members of the Board of Directors. Each of our non-employee directors is entitled to receive \$10,000 other than the Chairman of the Board, who is entitled to receive \$25,000. In addition, the head of our Audit Committee receives \$5,000, and the heads of our Compensation and Governance Committees receive \$2,500 annually. Each director receives \$1,000 for board or committee meetings attended in person, or \$500 for meetings attended by teleconference. Board compensation is paid annually after the annual general meeting of shareholders. We also reimburse directors for expenses incurred on our behalf, including expenses associated with attendance at meetings of our Board of Directors. In 2003 it was established that new board members would receive an option to acquire 30,000 shares. After the 2003 annual general meeting, we granted existing board members an option to acquire 15,000 shares, other than the Chairman, who was awarded an option to acquire 25,000 shares. The Board agreed it would not receive an annual option grant in 2004.

### ***Compensation of the Chief Executive Officer***

Mr. Korpolski's 2003 base salary was determined based on an evaluation of the salaries of Chief Executive Officers of comparable companies and Mr. Korpolski's experience, in accordance with the policies noted above. His bonuses have been determined based upon an evaluation of his performance against criteria established annually by the Compensation Committee and the Chairman of the Board based on the current circumstances of the Company, including the company's level of operations, financial position, development of HspE7, bioreagent sales, and operations within budget.

### **Compensation of Executive Officers**

The following table sets forth, in U.S. dollars, all compensation awarded or paid to and earned by, our Chief Executive Officer, the four most highly compensated executive officers who were serving as executive officers at the end of 2003 and an individual that became an executive officer in 2004 (collectively, the "Named Executive Officers") for services rendered during the years ended December 31, 2003, 2002 and 2001.

**Summary Compensation Table, in U.S. Dollars**

Name and Principal Position	Year	Annual compensation			Long term compensation
		Salary	Bonus	Other Compensation	Securities Underlying Options
Daniel L. Kopolinski President and Chief Executive Officer	2003	\$395,200	-- <sup>(1)</sup>	\$106,269 <sup>(2)</sup>	150,000 <sup>(9)</sup>
	2002	380,000	136,800	143,832 <sup>(2)</sup>	100,000
	2001	364,583	128,625	125,131 <sup>(2)</sup>	--
Howard T. Holden, Ph.D. Vice President, Regulatory Affairs and Compliance	2003	\$270,300	-- <sup>(1)</sup>	--	30,000 <sup>(9)</sup>
	2002	132,500 <sup>(3)</sup>	63,125 <sup>(4)</sup>	--	100,000
Gregory M. McKee Vice President, Corporate Development and Chief Financial Officer	2003	\$135,312 <sup>(5)</sup>	-- <sup>(1)</sup>	\$28,823 <sup>(6)</sup>	175,000
John R. Neefe, M.D. Senior Vice President, Clinical Research	2003	\$294,600	-- <sup>(1)</sup>	--	50,000 <sup>(9)</sup>
	2002	286,000	60,000	--	50,000
	2001	275,000	68,750	--	50,000
Marvin I. Siegel, Ph.D. Executive Vice President, Research and Development	2003	\$269,400	-- <sup>(1)</sup>	\$1,983 <sup>(7)</sup>	30,000 <sup>(9)</sup>
	2002	261,500	42,500	2,078 <sup>(7)</sup>	30,000
	2001	251,450	50,290	--	50,000
Donald D. Tartre Former Vice President and Chief Financial Officer	2003	\$241,800	--	--	50,000 <sup>(9)</sup>
	2002	232,500	50,000	--	40,000
	2001	185,795 <sup>(8)</sup>	46,875	--	200,000

- (1) Amounts exclude bonuses, if any, which the compensation committee may award based on the performance of the named executive officers from January 1, 2003 through December 31, 2003.
- (2) Amount includes medical premiums, life insurance premiums, housing and automobile costs, and amounts paid under Mr. Kopolinski's contract to compensate for the differential between the Canadian and U.S. effective tax rates.
- (3) Dr. Holden commenced employment on July 1, 2002.
- (4) Amount includes a \$30,000 signing bonus and a \$33,125 bonus granted in February 2003 relating to Dr. Holden's performance from July 1, 2002 through December 31, 2002.
- (5) Mr. McKee commenced employment on June 9, 2003.
- (6) Amount includes relocation costs.
- (7) Amount includes long-term disability premiums.

(8) Mr. Tartre commenced employment on March 5, 2001.

(9) Granted in 2003 based on 2002 performance.

### Stock Option Grants and Exercises in Last Fiscal Year

We grant options to our executive officers to purchase our common stock under our 2001 Equity Incentive Plan. Once the 2001 Plan was approved by our shareholders, we ceased to grant options under our 1996 Share Incentive Plan. As of December 31, 2003, options to purchase a total of 3,137,065 shares were issued and outstanding under the 2001 Plan and 1,841,053 shares were outstanding under the 1996 Plan. Options to purchase 358,986 shares remained available for grant under the 2001 Plan. The following table sets forth certain information regarding options granted during the fiscal year ended December 31, 2003 to the Named Executive Officers:

Name	Individual Grants				Potential Realizable Value at Assumed Annual Rates of Stock Appreciation for Option Term (Cdn. \$)	
	Shares Underlying Options Granted (#)	% of Total Options Granted to Employees in Fiscal Year (%)	Exercise Price Per Share (Cdn. \$)	Expiration Date	5%	10%
Daniel L. Korpolinski	150,000 (1)	14%	\$1.63	2/4/2013	\$153,765	\$389,670
Howard T. Holden, Ph.D.	30,000 (1)	3%	\$1.63	2/4/2013	30,753	77,934
Gregory M. McKee	175,000 (2)	17%	\$2.60	6/8/2013	286,147	725,153
John Neefe, M.D.	50,000 (1)	5%	\$1.63	2/4/2013	51,255	129,890
Donald D. Tartre	50,000 (1)	5%	\$1.63	2/4/2013	51,255	129,890
Marvin I. Siegel, Ph.D.	30,000 (1)	3%	\$1.63	2/4/2013	30,753	77,934

(1) Such options vest 1/36<sup>th</sup> per month over a 36 month period on the monthly anniversary of the vesting commencement date.

(2) Such options vest 1/4<sup>th</sup> on June 9, 2004, then 1/48<sup>th</sup> per month over the following 36 months

### Aggregated Option Exercises in Last Fiscal Year And Fiscal Year-End Option Values

The following table sets forth certain information as of December 31, 2003, regarding options held by the Named Executive Officers. There were no stock appreciation rights outstanding on December 31, 2003.

Name	Shares Acquired on Exercise	Aggregate Value Realized (Cdn. \$)	Number of Shares Underlying Unexercised Options at FY-End (#)		Value of Unexercised In-The-Money Options as of FY-End (Cdn. \$)	
			Exercisable	Unexercisable	Exercisable	Unexercisable
Daniel L. Korpilinski	--	--	1,046,179	203,821	\$67,916	\$176,584
Howard T. Holden, Ph.D.	--	--	43,749	86,251	\$13,583	\$35,317
Gregory M. McKee	--	--	--	175,000	--	--
John R. Neefe, M.D.	56,667	\$ 93,501	140,832	54,168	\$22,637	\$58,863
Marvin I. Siegel, Ph.D.	--	--	122,499	32,501	\$13,583	\$35,317
Donald D. Tartre	--	--	163,053	126,947	--	--

### **Employment Contracts and Termination of Employment and Change-in-Control Arrangements**

Our President and Chief Executive Officer, Daniel L. Korpilinski, is employed under an employment agreement dated March 8, 2000. In addition to his 2003 base salary of U.S. \$395,200, the agreement specifies that Mr. Korpilinski is eligible to receive additional incentive compensation of up to 40% of his base salary in any 12 month fiscal year if he meets individual objectives established annually by the board of directors. In the event that Mr. Korpilinski is terminated without just cause, he is entitled to severance payments equal to 12 months' base salary. Mr. Korpilinski is also entitled to severance payments equal to 12 months' base salary in the event that, within 12 months after an acquisition of more than 50% of our issued voting shares, Mr. Korpilinski is terminated or experiences a change in his title or responsibilities. Within 6 months after such a change in control, if Mr. Korpilinski terminates the employment agreement, he is entitled to severance payments equal to 12 months' of his current base salary. Mr. Korpilinski's stock option agreement under the 2001 Plan provides that the vesting and exercisability of his options will accelerate in full in the event his employment is involuntarily terminated without cause or voluntarily terminated for specified reasons within twenty-four (24) months after a specified change in control. Stock options granted under the 1996 Plan become fully exercisable after a specified change in control. Stressgen rents a condominium in San Diego for Mr. Korpilinski for U.S. \$2,650 per month and reimburses him approximately U.S. \$5,000 per year for supplemental life insurance, together with income taxes on such amounts.

Dr. Howard Holden, our Vice President, Regulatory Affairs and Compliance, is employed under an agreement dated May 8, 2002. In 2003, Dr. Holden received a base salary of U.S. \$270,300 under this agreement. He also is eligible for a bonus of up to 25% of his base salary, depending upon the achievement of corporate goals and the measure of his individual performance. In the event that Dr. Holden is terminated without cause, he is entitled to 6 months of severance payments. Dr. Holden is also entitled to 12 months of severance payments in the event of termination or significant change in title or responsibilities within 12 months after a specified change in control. Dr. Holden's stock option agreements under the 2001 Plan provide that the vesting and exercisability of his options will accelerate in full in the event his employment is involuntarily terminated without cause or voluntarily terminated for specified reasons within 24 months after a specified change in control.

Mr. Gregory McKee, our Vice President, Corporate Development and Chief Financial Officer, is employed under an agreement dated June 9, 2003. In 2003, Mr. McGee received a base salary of U.S. \$205,000 under this agreement; he also received a relocation allowance of up to U.S. \$30,000. Mr. McKee is eligible for a bonus of up to 25% of his base salary, depending upon the achievement of corporate goals and the measure of his individual performance. In the event that Mr. McKee is terminated without cause, he is entitled to 9 months of severance payments. Mr. McKee is also entitled to severance payments equal to 9 months base salary in the event of a termination or constructive termination within two years after a change in control. Mr. McKee stock option agreements under the 2001 Plan provide that the vesting and exercisability of his options will accelerate in full in the event his employment is involuntarily terminated without cause or voluntarily terminated for specified reasons within 24 months after a specified change in control.

Our Senior Vice President, Clinical Research, John R. Neefe, M.D., is employed under an employment agreement dated December 14, 1998, as amended on December 16, 1999. In 2003 Dr. Neefe's base salary was U.S. \$294,600 under this agreement; he also is eligible for a bonus of up to 20% of his base salary based on performance. In order to terminate Dr. Neefe's employment for other than just cause, we must provide Dr. Neefe with 12 month' prior notice. Dr. Neefe is also entitled to severance payments equal to his last two years' compensation in the event of termination within 12 months' after a change in ownership of our common stock within any 3 month period of at least 50% which results in a change in the majority of the members of our Board. Dr. Neefe's stock option agreements under the 2001 Plan provide that the vesting and exercisability of his options will accelerate in full in the event his employment is involuntarily terminated without cause or voluntarily terminated for specified reasons within 24 months after a specified change in control. Stock options granted under the 1996 Plan become fully exercisable after a specified change in control.

Marvin I. Siegel, Ph.D., our Executive Vice President, Research and Development, is employed under an employment agreement dated February 5, 1997, as amended on January 11, 1999. In 2003 Dr. Siegel's base salary was U.S. \$269,400 under this agreement; he also is eligible for a bonus based on exemplary service and supplemental disability insurance. In the event that Dr. Siegel is terminated without cause, he is entitled to 12 months notice or severance payments. Dr. Siegel is also entitled to severance payments equal to 24 months base salary in the event of termination within 12 months after an acquisition of more than 50% of our outstanding shares as a result of which a majority of the members of our Board change within 3 months. Dr. Siegel's stock option agreements under the 2001 Plan provide that the vesting and exercisability of his options will accelerate in full in the event his employment is involuntarily terminated without cause or voluntarily terminated for specified reasons within 24 months after a specified change in control. Stock options granted under the 1996 Plan become fully exercisable after a specified change in control.

Our Vice President and Chief Financial Officer, Donald D. Tartre, was employed under an employment agreement dated March 5, 2001, under which he was eligible for a base salary of \$241,800 in 2003 and a bonus of up to 25% of his base salary, depending upon the achievement of corporate goals and the measure of his individual performance. Mr. Tartre left Stressgen on January 14, 2004.

Subject to the *Business Corporations Act* (Yukon Territory), if specific preconditions are met, we will indemnify persons including a director, officer, former director or officer, person who has undertaken any liability on behalf of the corporation, and his or her heirs against losses reasonably incurred by reason of such status. Indemnification covers losses, charges and expenses incurred as a result of actions in such capacities. We are also empowered under our By-laws and the BCA (Yukon Territory) to purchase insurance on behalf of any person who we are required or permitted to indemnify. Pursuant to this provision, we currently maintain directors and officers insurance coverage. In addition, we have entered into indemnity agreements with our directors and officers and intend to enter into similar agreements with future directors and officers. These agreements could require us to indemnify those officers and directors against liabilities that arise by reason of their status or service as officers or directors. In certain circumstances the agreements would also require us to advance the expenses an officer or director incurs in legal proceedings. We believe that the provisions in our By-laws and contractual indemnification are necessary to attract and retain qualified persons as directors and officers. At present, there is no pending litigation or proceeding involving any of our directors, officers, employees or agents where indemnification will be required or permitted. We are not aware of any threatened litigation or proceeding that may result in a claim for indemnification.

**Item 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT**

The following table sets forth information as of January 31, 2003 with respect to (i) each stockholder known to us to be the beneficial owner of more than 5% of our outstanding common stock, (ii) each director, (iii) our Chief Executive Officer, our four most highly compensated executive officers other than the Chief Executive Officer who were serving as executive officers at the end of the last completed fiscal year and an individual who was not serving as an executive officer of the registrant at the end of the last completed fiscal year but who currently is one of our four most highly compensated executive officers other than the Chief Executive Officer (together, the "Named Executive Officers") and (iv) all of our directors and executive officers as a group. Except as set forth below, each of the named persons has sole voting and investment power with respect to the shares shown.

<u>Beneficial Owner of Common Stock (1)</u>	<u>Amount and Nature of Beneficial Ownership of Common Stock (2)(3)</u>	<u>Percent of Class of Common Stock (2)(3)</u>
Roche Finance Ltd. Grenzacherstrasse 124, CH – 4070 Basel, Switzerland.....	4,392,436(4)	6.0%
FMR Corp. 82 Devonshire Street Boston, MA 02109.....	6,694,170(5)	9.2%

<u>Beneficial Owner of Common Stock (1)</u>	<u>Amount and Nature of Beneficial Ownership of Common Stock (2)(3)</u>	<u>Percent of Class of Common Stock (2)(3)</u>
RBC Asset Management, Inc. Royal Trust Tower, Suite 3800 P.O. Box 121, Toronto Dominion Centre 77 King Street West Toronto, ON M5K 1H4		
Canada .....	8,641,400	11.9%
Joann L. Data, M.D., Ph.D. ....	55,000	*
Ian Lennox .....	53,333	*
Kenneth Galbraith (6) .....	100,000	*
Elizabeth Greetham.....	40,000	*
Margot Northey.....	41,666	*
Jay M. Short, Ph.D (7).....	117,000	*
Daniel L. Korpilinski .....	1,134,332	1.5%
Howard Holden, Ph.D.....	55,415	*
John R. Neefe, M.D. ....	160,276	*
Marvin I. Siegel, Ph.D .....	146,165	*
Donald D. Tartre .....	50,000	*
All Directors and Executive Officers as a Group (12 persons).....	1,953,187	2.6%

\*Less than one percent

- (1) This table is based upon information known to Stressgen or supplied by its officers, directors and principal shareholders. Except as shown otherwise in the table, the address of each person listed is in the care of Stressgen Biotechnologies, Inc., 6055 Lusk Boulevard, San Diego, California 92121.
- (2) Except as otherwise indicated in the footnotes of this table and pursuant to applicable community property laws, the persons named in the table have sole voting and investment power with respect to all shares of common stock. Beneficial ownership is determined in accordance with the rules of the Commission and generally includes voting or investment power with respect to securities. Shares of common stock subject to options or warrants exercisable within 60 days of February 12, 2004 are deemed outstanding for computing the percentage of the person or entity holding such options or warrants but are not deemed outstanding for computing the percentage of any other person.
- (3) In the case of the individuals listed below, the number of shares beneficially owned includes a specified number of shares issuable upon exercise of stock options exercisable within 60 days of February 12, 2004: Dr. Data (55,000); Mr. Lennox (53,333); Mr. Galbraith (85,000); Ms. Greetham (40,000); Ms. Northey (41,666); Dr. Short (95,000); Mr. Korpilinski (1,133,332); Dr. Holden (55,415); Dr. Neefe (151,943); Dr. Siegel (129,165); and Mr. Tartre (50,000). Percentage of beneficial ownership is based upon 72,491,403 shares of our common stock deemed outstanding as of February 12, 2004.
- (4) Includes 2,036,436 common shares and up to 2,356,000 common shares issuable upon the exercise of a warrant, which Roche Finance Ltd. may exercise in its discretion through June 28, 2007.
- (5) Represents holdings by FMR Corp. and its directly and indirectly owned subsidiaries, in the context of passive investment activities only, for the investment accounts they manage on a discretionary basis.
- (6) Mr. Galbraith disclaims beneficial ownership of 15,000 shares of common stock, which are held by Mrs. Shelley Galbraith on behalf of two minor children.

- (7) Mr. Short disclaims beneficial ownership of 22,000 shares of common stock, which are held by the Ryco 2001 Family Trust on behalf of Mr. Short and his immediate family.

### **Item 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS**

None.

### **Item 14. PRINCIPAL ACCOUNTING FEES AND SERVICES**

The information presented below is denominated in U.S. dollars unless otherwise noted.

#### **Audit Fees**

During the years ended December 31, 2003 and 2002, we paid Deloitte & Touche LLP ("Deloitte") aggregate fees and related expenses for the audit of our financial statements for the year and for the reviews of the our interim financial statements of approximately \$108,000 and \$106,000, respectively. Of these amounts, \$20,000 and \$10,000 related to translation services performed in 2003 and 2002 respectively.

#### **Audit-Related Fees**

We paid Deloitte approximately \$4,000 and \$16,000 during the years ended December 31, 2003 and 2002, respectively, related to audit-related services.

#### **Tax Fees**

During the years ended December 31, 2003 and 2002, we paid Deloitte aggregate fees and related expenses of \$64,000 and \$46,000 for preparation of our income tax returns and other tax consulting.

#### **All Other Fees**

We incurred fees for other professional services rendered by Deloitte of approximately \$57,000 and \$58,000 during the years ended December 31, 2003 and 2002, respectively. In 2003, these services related primarily to support of our fourth quarter equity offering. In 2002, these services primarily related to design and implementation of global tax strategies.

Generally, before we engage Deloitte to render audit or non-audit services, the engagement is approved by our audit committee. Our audit committee reviews written engagement letters prepared by Deloitte for engagements such as the annual audit. It has also pre-approved the engagement of Deloitte for tax matters including the preparation of federal, provincial and state income tax returns pursuant to specific pre-approval guidelines established by the audit committee. In 2003, 26% of the services were approved by the audit committee retroactively. Management engaged Deloitte to perform these services in compliance with audit committee policy, and informed the audit committee of each such service thereafter.

## PART IV

### Item 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES AND REPORTS ON FORM 8-K

#### (1) Financial Statements

Our financial statements are included herein under Item 8 of this Annual Report on Form 10-K.

#### (2) Financial Statement Schedules

Financial statement schedules have been omitted since they are either not required, not applicable, or the information is otherwise included.

#### (3) Exhibits

Exhibit No.	Description
3.9*	Articles of Continuance of the Company
3.10*	By-Laws of the Company
4.4*	Form of Stock Certificate
10.1**	License Agreement dated November 29, 1992 among Whitehead Institute for Biomedical Research, MIT and the Company, as amended
10.2**	Lease for the Company's offices in Victoria, British Columbia
10.3**	Employment Agreement dated March 8, 2000 between the Company and Daniel Korpolinski
10.10**	1996 Share Incentive Plan
10.12***	2001 Equity Incentive Plan
10.13+	Articles of Continuance of the Company
10.15	Restructured and Restated HspE7 Collaboration Agreement dated December 1, 2003 among the Company, Stressgen Development Corporation, F.Hoffmann-La Roche Ltd. and Hoffmann-La Roche Inc.
21.3++	List of Subsidiaries
23.1	Independent Auditors' Consent
24.1	Power of Attorney (Included on the signature page of this Annual Report on Form 10-K)
31.1	Rule 13a-14(a)/15d-14(a) Certification of Chief Financial Officer
31.2	Rule 13a-14(a)/15d-14(a) Certification of Chief Executive Officer
32	Section 1350 Certification

\* Incorporated by reference to the Company's Form 10-Q for the quarter ended June 30, 2001, as filed with the Commission on August 2, 2001

\*\* Incorporated by reference to the Company's Form 10-K for the year ended December 31, 2000, as filed with the Commission on April 2, 2001

\*\*\* Incorporated by reference to Exhibit 99.1 of the Company's Registration Statement on Form S-8, as filed with the Commission on May 30, 2001

+ Incorporated by reference to the Company's Form 10-K for the year ended December 31, 2001, as filed with the Commission on March 19, 2002

++ Incorporated by reference to the Company's Form 10-K for the year ended December 31, 2002, as filed with the Commission on February 10, 2003

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

On December 2, 2003 we filed with the Securities and Exchange Commission a report on Form 8-K describing under "Item 5 – Other Events" our restructured collaboration agreement with Roche.

**Supplemental Information to be Furnished with Reports Filed Pursuant to Section 15(d) of the Act by Registrants Which Have Not Registered Securities Pursuant to section 12 of the Act.**

As of the date hereof, no annual report for the 2003 fiscal year or proxy materials have been sent to our shareholders. An annual report and proxy materials will be furnished to shareholders and the Securities and Exchange Commission on or about April 12, 2004.

**SIGNATURES**

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

STRESSGEN BIOTECHNOLOGIES CORPORATION

Date: February 19, 2004

BY: /s/ Daniel L. Kopolinski  
Daniel L. Kopolinski  
President and Chief Executive Officer

## POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Daniel L. Kopolinski and Gregory M. McKee, as his true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him and in his name, place and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and full power and authority to do and performance each and every act and thing requisite and necessary to be done in connection therewith, as fully to intents and purposes as he might or could do in person, hereby ratifying and confirming that all said attorneys-in-fact and agents, or any of them or their or his substitute or resubstitute, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this report has been signed below by the following person on behalf of the Registrant and in the capacities and on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Daniel L. Kopolinski</u> Daniel L. Kopolinski	Chief Executive Officer, President and Director <i>(Principal Executive Officer)</i>	February 19, 2004
<u>/s/ Gregory M. McKee</u> Gregory M. McKee	Vice President, Corporate Development and Chief Financial Officer <i>(Principal Financial and Accounting Officer)</i>	February 19, 2004
<u>/s/ Joann L. Data</u> Joann L. Data, M.D., Ph.D.	Director	February 19, 2004
<u>/s/ Kenneth Galbraith</u> Kenneth Galbraith	Director	February 19, 2004
<u>/s/ Elizabeth Greetham</u> Elizabeth Greetham	Director	February 19, 2004
<u>/s/ Ian Lennox</u> R. Ian Lennox	Chairman of the Board of Directors	February 19, 2004
<u>/s/ Margot Northey</u> Margot Northey	Director	February 19, 2004
<u>/s/ Jay Short</u> Jay Short	Director	February 19, 2004

**INDEPENDENT AUDITORS' CONSENT**

We consent to the incorporation by reference in Registration Statement No. 333-61900 of Stressgen Biotechnologies Corporation on Form S-8 of our report dated February 12, 2004, appearing in this Annual Report on Form 10-K of Stressgen Biotechnologies Corporation for the year ended December 31, 2003.

/s/ Deloitte & Touche LLP  
San Diego, California  
February 19, 2004

## CERTIFICATION

I, Gregory M. McKee, certify that:

1. I have reviewed this annual report on Form 10-K of Stressgen Biotechnologies Corporation (the "company");
2. Based on my knowledge, this 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 report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the company as of, and for, the periods presented in this report;
4. The company's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the company and have:
  - a. designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - b. evaluated the effectiveness of the company's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation;
  - c. disclosed in this report any change in the company's internal control over financial reporting that occurred during the company's most recent fiscal quarter that has materially affected or is reasonably likely to materially affect, the company's internal control over financial reporting; and
5. The company's other certifying officers and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the company's auditors and the audit committee of company's board of directors (or persons performing the equivalent function):
  - a. all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the company's ability to record, process, summarize and report financial information; and
  - b. any fraud, whether or not material, that involves management or other employees who have a significant role in the company's internal control over financial reporting.

Date: February 19, 2004

/s/ Gregory M. McKee  
Gregory M. McKee  
Vice President, Corporate Development and  
Chief Financial Officer

## CERTIFICATION

I, Daniel L. Kopolinski, certify that:

1. I have reviewed this annual report on Form 10-K of Stressgen Biotechnologies Corporation (the "company");
2. Based on my knowledge, this 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 report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the company as of, and for, the periods presented in this report;
4. The company's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the company and have:
  - a. designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - b. evaluated the effectiveness of the company's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation;
  - c. disclosed in this report any change in the company's internal control over financial reporting that occurred during the company's most recent fiscal quarter that has materially affected or is reasonably likely to materially affect, the company's internal control over financial reporting; and
5. The company's other certifying officers and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the company's auditors and the audit committee of company's board of directors (or persons performing the equivalent function):
  - a. all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the company's ability to record, process, summarize and report financial information; and
  - b. any fraud, whether or not material, that involves management or other employees who have a significant role in the company's internal control over financial reporting.

Date: February 19, 2004

/s/ Daniel L. Kopolinski  
Daniel L. Kopolinski  
President and Chief Executive Officer

Certification Pursuant to 18 U.S.C. § 1350  
as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

In our capacities as President and Chief Executive Officer and Vice President and Chief Financial Officer of Stressgen Biotechnologies Corporation (the "Company") we hereby certify based on our respective knowledge that: (a) the enclosed Annual Report on Form 10-K for the period ended December 31, 2003 as filed with the Securities and Exchange Commission on the date hereof fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934 and (b) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

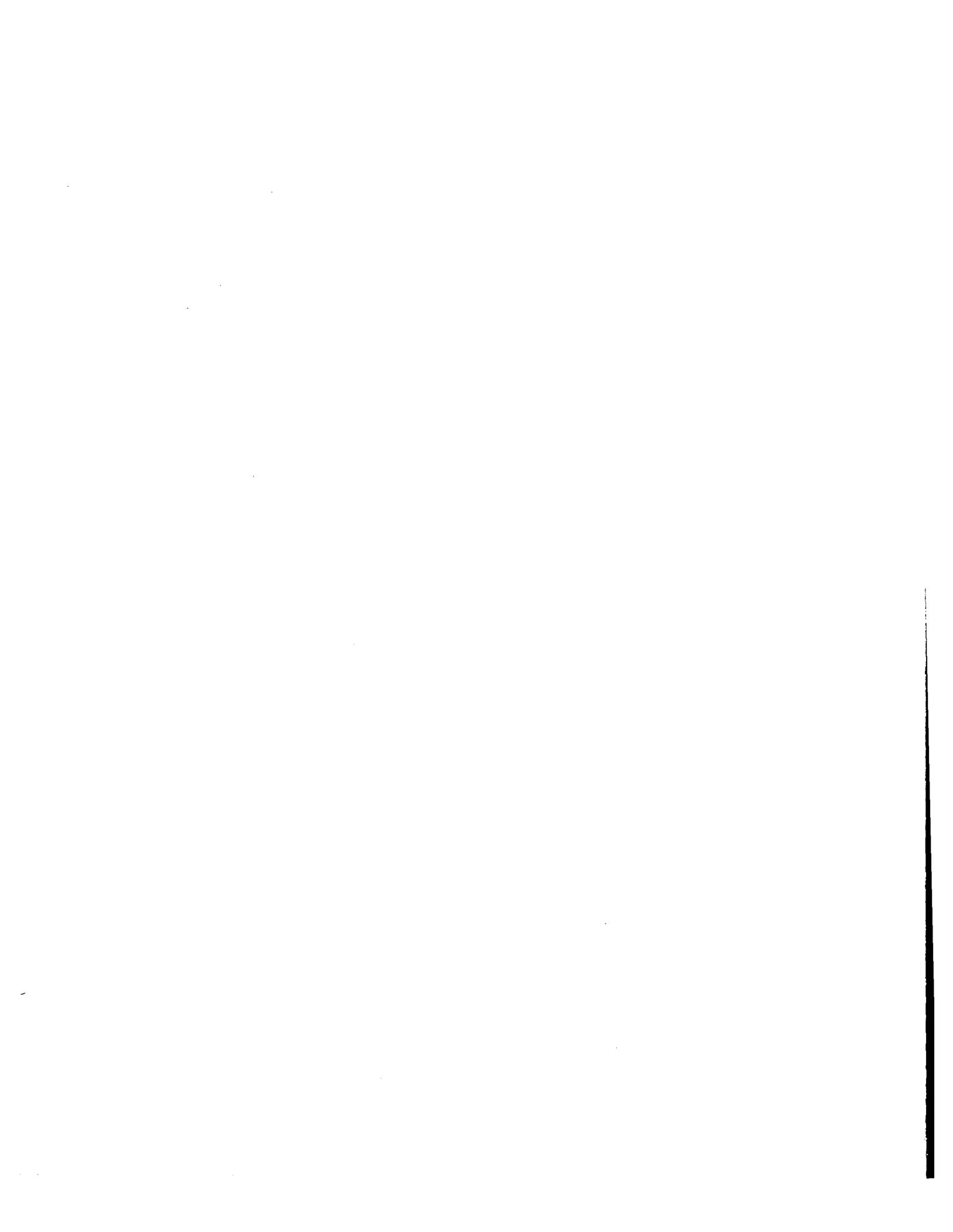
February 19, 2004

/s/Daniel L. Korpilinski

Daniel L. Korpilinski  
President and Chief Executive Officer

/s/ Gregory M. McKee

Gregory M. McKee  
Vice President, Corporate Development and Chief  
Financial Officer



# Corporate Directory

## Management

**Daniel L. Kopolinski**  
President & Chief Executive Officer

**Gregory M. McKee**  
Vice President, Corporate Development and  
Chief Financial Officer

**Marvin I. Siegel, Ph.D.**  
Executive Vice President, Research & Development

**John R. Neefe, M.D.**  
Senior Vice President, Clinical Development

**Howard T. Holden, Ph.D.**  
Vice President, Regulatory Affairs and Compliance

**Lee Mizzen, Ph.D.**  
Vice President, Scientific Affairs

**Bruce M. Berger, M.D.**  
Vice President, Clinical Development

**Ariel Louwrier, Ph.D.**  
Director, Operations-Bioreagents

## Board of Directors

**Joann Data, M.D., Ph.D.<sup>1,3</sup>**  
Senior Vice President, Regulatory Affairs  
and Quality Assurance  
Amylin Pharmaceuticals

**Kenneth Galbraith, CA<sup>2</sup>**  
Current President  
Gigha Consulting Ltd.  
Former Executive Vice President & CFO  
QLT Inc.

**Elizabeth Greetham, B.Sc., M.A.<sup>2</sup>**  
Current President  
ACCL Financial Consultants  
Former Chairman & Chief Executive Officer  
DrugAbuse Sciences, Inc.

**Daniel L. Kopolinski**  
President & Chief Executive Officer  
Stressgen Biotechnologies Corporation

**Ian Lennox<sup>1,2</sup>**  
President & Chief Executive Officer  
Drug Discovery & Development Sector  
MDS Inc.

**Margot Northey, Ph.D., M.A.<sup>3</sup>**  
Former Dean of Queen's School of Business  
Queen's University  
Kingston, Ontario

**Jay M. Short, Ph.D.<sup>1</sup>**  
President & Chief Executive Officer  
Diversa Corporation

(1) Compensation Committee

(2) Audit Committee

(3) Governance Committee





**Stressgen**  
BIOTECHNOLOGIES

**Canadian Office:**

Stressgen Biotechnologies Corporation  
350-4243 Glanford Avenue  
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Telephone: 250-744-2811  
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**Principal Executive Office:**

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6055 Lusk Boulevard  
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# Corporate Directory

## Management

**Daniel L. Kopolinski**

President & Chief Executive Officer

**Gregory M. McKee**

Vice President, Corporate Development and  
Financial Officer

**Marvin J. Siegel, Ph.D.**

Executive Vice President, Research & Development

**Tom R. Neefe, M.D.**

Senior Vice President, Clinical Development

**Howard T. Holden, Ph.D.**

Vice President, Regulatory Affairs and Compliance

**Lee Mizzen, Ph.D.**

Vice President, Scientific Affairs

**Bruce M. Berger, M.D.**

Vice President, Clinical Development

**Wendy Louwrier, Ph.D.**

Director, Operations-Bioreagents

## Board of Directors

**Joann Data, M.D., Ph.D.<sup>1,3</sup>**

Senior Vice President, Regulatory Affairs  
and Quality Assurance  
Smith Pharmaceuticals

**Kenneth Galbraith, CA<sup>2</sup>**

Current President  
Sigma Consulting Ltd.  
Former Executive Vice President & CFO  
ATI Inc.

**Elizabeth Greenham, B.Sc., M.A.<sup>2</sup>**

Current President  
E.C.I. Financial Consultants  
Former Chairman & Chief Executive Officer  
EpiAbuse Sciences, Inc.

**Daniel L. Kopolinski**

President & Chief Executive Officer  
Amgen Biotechnologies Corporation

**Jan Lennox<sup>1,2</sup>**

President & Chief Executive Officer  
Drug Discovery & Development Sector  
Pfizer Inc.

**Margot Northey, Ph.D., M.A.<sup>3</sup>**

Former Dean of Queen's School of Business  
Queen's University  
Kingston, Ontario

**Ray M. Short, Ph.D.<sup>1</sup>**

President & Chief Executive Officer  
Amgen Corporation

— Nominations Committee

— Audit Committee

— Compensation Committee

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]



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