Medgenics Inc. ("Medgenics" or "the Company") is a closely held biopharmaceutical company developing a platform technology to provide sustained-action protein therapy for the treatment of a range of diseases, starting with anemia† and hepatitis C. As an alternative to today’s protein therapy which involves frequent bolus injections of proteins, Medgenics is developing a biological pump, called the Biopump, made using the patient’s own skin. Directly addressing the majority of the $51 billion market for injected proteins, the Biopump works inside a patient’s body to produce and deliver the active protein steadily for a sustained duration in order to treat a targeted indication. The Biopump platform employs a sliver of dermal tissue, which is harvested from under a patient’s skin and engineered to manufacture and distribute the required therapeutic protein. Dermal tissue is processed ex vivo and transduced with a viral vector having non-immunogenic properties, which carries the appropriate gene into the nuclei of the tissue’s cells and causes the cells to produce the selected protein, converting the dermal tissue into a sustained-action Biopump. Ten days after the initial harvest, the Biopump is implanted back into the patient, where it is designed to supply the active protein to the patient for at least four to six months. The Biopump creates a protein production plant within the patient, intended to alleviate the need for frequent, costly, and painful injections and to avoid their side effects. Medgenics has already shown proof-of-principle of the Biopump to deliver erythropoietin (EPO) in a clinical trial to anemic patients, and has demonstrated semi-automated devices that when fully developed, may enable safe, reliable, and cost-effective implementation of the method at local clinics. The Company is developing two products based on its sustained-action Biopump technology: EPODURE producing EPO to treat anemia, and INFRADURE producing interferon-alpha (IFN-α) to treat hepatitis C. Medgenics plans to commence efficacy trials for EPODURE within 12 months. The Company believes its Biopump platform is able to provide a pipeline of sustained-action protein drugs capable of offering treatment for a range of other illnesses/conditions, such as multiple sclerosis (MS), hemophilia, pediatric growth deficiencies, muscle atrophy, cancer, obesity, wound healing, diabetes, arthritis, and others. Medgenics is a U.S.-based company with a wholly owned subsidiary, Medgenics Medical Israel, Inc., in Karmiel, Israel.

Key Points

- Medgenics’ proprietary Biopump platform technology converts dermal tissue into an internal protein production plant through ex vivo transduction with a viral vector and re-implantation of the patient’s own tissue under the skin. The technology is developed to produce and deliver natural therapeutic proteins on a sustained basis versus the current standard of high quantity, costly, and painful injections.
- The protein therapeutic market was valued at over $51 billion in 2005 and is forecast to reach $87 billion by 2010, according to Kalorama Information (www.kaloramainformation.com, a division of www.marketresearch.com), due to heavy demand and rapid sales in the U.S. and Europe. Medgenics’ technology targets the majority of this market for protein injection therapy. As a point of reference, in 2005, patients received more than $11 billion worth of EPO injections to treat anemia, and more than $3.5 billion worth of IFN-α to treat hepatitis C and some forms of cancer.
- Medgenics has demonstrated clinical proof-of-principle for its short-action Biopump system (capable of lasting 14 days) producing and delivering EPO to patients suffering from anemia, and has confirmed laboratory and mouse performance of its next-generation, sustained-action Biopump system (capable of lasting at least four to six months) for both EPO and IFN-α in anemia and hepatitis C, respectively.
- Medgenics’ technology is versatile and could allow for the development of an array of applications. Many disease targets in which the technology can be applied represent multi-billion dollar opportunities.
- Medgenics’ technology is protected by 48 patents and patent applications, including one issued U.S. patent, nine pending U.S. applications, one issued foreign patent, and 37 pending foreign applications.
- Medgenics is managed by a team of individuals with decades of experience in biotechnology and biomedical devices and professionals from the healthcare, finance, medical, and academic fields. The Board of Directors includes current and former directors of international healthcare companies, and the Scientific Advisory Board (SAB) includes past presidents of the Renal Physicians Association, the American Gastroenterological Association, and the American Society of Gene Therapy.
- Dr. Andrew Pearlman, the Company’s founder and current chief executive officer (CEO), raised Medgenics’ $17 million in funding in four equity rounds, and took the Company through its first clinical trial. Medgenics is currently working to raise funds to complete preparations for its Phase II/III efficacy trials of EPODURE to treat anemia, expected to commence in fourth quarter 2007 and INFRADURE to treat hepatitis C, expected to commence in first quarter 2008.

†BOLD WORDS ARE REFERENCED IN GLOSSARY ON PAGES 46-49.
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Executive Overview

Medgenics Inc. (“Medgenics” or “the Company”) is a closely held biopharmaceutical company developing a unique sustained-action therapeutic protein delivery technology for the treatment of a range of diseases. As an alternative to bolus injections of mass-produced proteins from animal cells (predominantly rodent cells), Medgenics is developing a biological pump, called the Biopump, which is made from a sliver of the patient’s own skin and works inside the patient’s body to produce and deliver the active protein steadily for a sustained duration in order to treat the targeted indication. The Company’s Biopump creates a protein production plant within the patient. Medgenics currently has two products in development based on its Biopump platform technology: EPODURE producing erythropoietin (EPO) to treat anemia and INFRADURE utilizing interferon-alpha (IFN-α) to treat hepatitis C.

Medgenics’ Technology

The Company’s Biopump platform technology works by utilizing a specialized, proprietary extractor to remove a micro-organ (MO)—a sliver of dermal tissue—from the dermal layer of the patient’s skin using a local anesthetic in a physician’s clinic. The MO is inserted into a self-standing ex vivo processing station, which transforms the MO into a tested Biopump within 10 days using a viral or non-viral vector that has been engineered to carry the gene that codes for the therapeutic protein but will not activate the immune system. Production of the target protein from the therapeutic gene begins once the vector has been absorbed by the cells. After measuring the levels of protein produced, the Biopump is reinserted into the patient, where it is designed to continue to supply the active therapeutic protein on a sustained basis for at least four to six months. This compares to just a few days or a week for the best protein therapies available today. The sustained-action Biopump has been designed to alleviate the need for a continuous cycle of high quantity, costly, and painful bolus injections, which can result in peak and trough protein levels within the blood. Figure 1 is a fundamental overview of the stages of the Biopump procedure.

A key step of the ex vivo processing for the conversion of the MOs from the patient into functional Biopumps is to be performed in a sealed cassette for each patient, using a semi-automated Biopump processing device, called the Bioreactor (detailed on page 17). In this manner, each patient’s MOs can be processed in a reliable, reproducible method in a sterile environment, while preventing cross contamination from other patients’ Biopumps being processed simultaneously. Medgenics has demonstrated the feasibility of a prototype Bioreactor converting MOs into Biopumps using single-use cassettes. Re-implantation into the patient via subcutaneous injection uses a special implantation device. Should it be necessary to stop the function of one or more implanted Biopumps, they can be ablated through surgical removal or by using adaptations of standard cautery needle or laser ablation methods.

Short-Action Biopump

Medgenics’ clinical proof-of-principle trial for its Biopump technology demonstrated a short-action version of the Biopump provided EPO therapy to patients with anemia. This Phase I trial in anemic patients with chronic kidney disease (CKD) showed safe, dose-controlled, and reproducible production and delivery of active EPO protein in these patients using Biopumps from the patients’ own skin. Pages 19-20 provide greater details on this trial. In parallel with the trial, Medgenics completed proof-of-principle prototypes of the devices used to implement the Biopump technology (Harvester, Implanter, Ablator, and Bioreactor).
Sustained-Action Biopump

The Company’s new-generation, sustained-action Biopump is designed to provide at least four to six months of protein therapy for a patient through a single injection session using new viral vectors with non-immunogenic properties. Studies in leading research centers have shown that these viral vectors can provide more than a year of steady protein production in immune-competent animals such as baboons and dogs. Using these new vectors, the Company has successfully and repeatedly produced scores of the new, long-acting human skin Biopumps from human dermis MOs. These sustained-action Biopumps have now reproducibly produced over five months of active protein at therapeutic levels in vitro. When these new sustained-action EPO Biopumps are implanted under the skin of Severe Combined Immunodeficient (SCID) mice, the hematocrit levels rise quickly, and remain elevated for months, indicating the sustained, continual production of active protein in vivo. The Company has also shown similar sustained in vitro production and in vivo delivery of IFN-α in such mice.

Medgenics is now collecting supportive preclinical data in advance of its next clinical trials in patients—to demonstrate the efficacy of EPODURE (sustained-action Biopump EPO) for use in treating anemia, and INFRADURE (sustained-action Biopump IFN-α) to treat hepatitis C. The Company plans to commence the anemia trial in Israel in the fourth quarter 2007 and the hepatitis C trial in the first quarter 2008.

Anemia

Anemia is a condition in which the number of red blood cells or the hemoglobin in the red blood cells is below normal. Hemoglobin is a red, iron-rich protein that gives blood its red color and enables red blood cells to carry oxygen from the lungs to all parts of the body and carry carbon dioxide to the lungs so that it can be exhaled. A person becomes anemic when the body produces too few healthy red blood cells, loses too many of them, or destroys them faster than they can be replaced. As a result, a person’s blood is too low in red blood cells to carry oxygen to their tissues, causing a number of symptoms, which may include weakness, pale skin, a fast heartbeat, shortness of breath, chest pain, dizziness, cognitive problems, numbness or coldness in the extremities, and headaches.

Initially, anemia can be so mild that it goes unnoticed; however, signs and symptoms increase as the condition evolves. Anemia is caused by, or associated with, a wide variety of conditions, ranging from chronic kidney disease (CKD) and end-stage renal disease (ESRD [dialysis patients]), to Acquired Immune Deficiency Syndrome (AIDS), hepatitis, cancer, chemotherapy, and other conditions. The National Kidney Foundation estimates the U.S. CKD population alone exceeds 20 million people, and that as many as 67 million people in the U.S. have hypertension and diabetes are at risk for CKD and subsequently anemia.

Erythropoietin (EPO) is a protein produced naturally in the kidneys that stimulates red blood cell production in the body. A shortage of EPO in the body, such as that caused by kidney disease, can cause anemia. EPO treatment has a short half-life, requiring three repeat injections per week, and each injection results in a temporary, massive overdose of EPO. In addition, patients frequently miss injections, resulting not only in the anemia being undertreated, but also often becoming unstable and difficult to manage.

Medgenics’ Solution: EPODURE

Medgenics is developing EPODURE to provide sustained therapy of anemia through continuous production and immediate delivery of EPO for at least four to six months from a single treatment using its sustained-action Biopump technology. The primary application for the Company’s technology is in anemia associated with CKD, though it may be used to treat anemia due to cancer, AIDS, or other indications.

Chronic Hepatitis C

Hepatitis is an inflammation of the liver usually caused by viral infections, toxic agents, or drugs, but may also result from an autoimmune response. Hepatitis C is caused by the hepatitis C virus (HCV). Worldwide, it is estimated that there are approximately 170 million chronic carriers, with three to four million new infections each year. Chronic HCV infection is the leading cause of liver disease in the U.S. and many other western countries.
Therapy for chronic hepatitis C involves 6 to 12 months of injections of IFN-α, which has anti-viral properties that prevent the entry of a virus into a cell and limit the amount of new cells that become infected, resulting in a greatly reduced HCV viral load in the patient. Like many therapeutic proteins, however, IFN-α has a short half-life, requiring two to three repeat injections per week, with each injection resulting in a temporary overdose of IFN-α. These often cause debilitating flu-like symptoms or more serious side effects such as depression, reduced white cell count, and others.

IFN-α has recently been reformulated into a pegylated molecule, peginterferon-α (PEG-IFN-α), which requires weekly injections. Even with PEG-IFN-α, a significant number of patients simply cannot tolerate the side effects. It is estimated that between 15% to 50% of patients drop out from the therapy, while many others are characterized as “slow responders” (i.e., fail to experience a viral load reduction after 12 weeks of standard therapy administered in combination with oral ribavirin—a pill to supplement interferon injections for HCV treatment). PEG-IFN-α, as currently used, is effective in only approximately 40% to 50% of selected patients. Therefore, there is a serious unmet medical need for a new form of interferon therapy for chronic hepatitis C with greatly reduced side effects and the same or increased efficacy compared to those of the bolus injections.

**Medgenics’ Solution: INFRADURE**

Medgenics is developing INFRADURE to provide at least four to six months of sustained-action IFN-α therapy from a single treatment using the Biopump platform technology to treat hepatitis C initially and potentially other indications in the future. Published studies have shown that steady delivery of IFN-α via infusion pump in hepatitis C patients provides effective therapy with far fewer side effects; however, such infusion pump delivery is not practical. Nevertheless, based on these studies and others, top hepatitis experts believe that INFRADURE, providing a steady release of IFN-α, could be an effective way to administer IFN-α therapy with far fewer side effects, offering a potentially significant advancement for all hepatitis C therapies and addressing the unmet need.

**Protein Therapeutic Market**

The protein therapeutic market was valued at over $51 billion in 2005 and is forecast to reach $87 billion by 2010, according to Kalorama Information, due to heavy demand and rapid sales in the U.S. and Europe. In 2005, patients received more than $11 billion worth of EPO injections to treat anemia, and patients treated with IFN-α for hepatitis C and some forms of cancer composed a $3.5 billion market.

Current protein therapeutics are mass-produced recombinant proteins commonly manufactured in animal cells (predominantly rodent cells) in large-scale current Good Manufacturing Practices (cGMP) production facilities. These proteins are subsequently purified and formulated for the human body before being delivered to the patient. The production facilities can be costly and time-consuming to build ($500 million to $1 billion) and can take several years to gain U.S. Food and Drug Administration (FDA) approval. In addition, recombinant proteins usually have a short half-life, so the amount of protein injected into a patient quickly diminishes. This can result in the need for frequent protein injections.

Longer lasting protein therapies using PEGylation—a process intended to lengthen the time a substance remains in the bloodstream without being metabolized and excreted by the body—still require injections at least every week, or in some cases every two weeks. Injecting larger protein doses can extend the life of the treatment, but the large concentrations can often cause adverse side effects. For example, many hepatitis C patients stop treatment altogether because the side effects are too severe, such as flu-like symptoms, depression, and reduction of white cell count.

Although nearly all protein therapeutics are delivered by injection, drug delivery companies are striving to develop alternative solutions to injections to deliver protein therapeutics. The protein delivery market is primarily immediate release, but there is a trend towards increased sustained release formulations. This being the case, the technology that Medgenics is developing with its sustained-action Biopump has demonstrated that it can exceed the duration of any current sustained-release formula. Medgenics plans to compete in these markets either through strategic partnerships or by establishing a stand-alone strategy to produce the sustained-action Biopumps and use them to provide improved protein therapy.
A technology such as the Biopump could become a novel addition to the field of protein therapeutics by providing the following benefits: eliminating the need for a protein production facility; eliminating the need for frequent injections; reducing side effects; increasing efficacy; lowering costs; extending treatment to undertreated populations; providing a simplified pathway to produce and deliver new and difficult to manufacture proteins; and offering a practical and reversible treatment option. These attributes and their accompanying benefits are described in greater detail on pages 28-29.

**Headquarters, Company History, and Employees**

Medgenics was founded in 2000 by its current chief executive officer (CEO) and president, Dr. Andrew Pearlman, as a Delaware corporation with major research and development (R&D) operations in Israel. The Israeli operations (shown in Figure 2) are Medgenics Medical Israel, Inc., based in Karmiel, which is a wholly owned subsidiary of Medgenics. The Company's U.S. location is located in Vienna, Virginia. The Company currently employs eight individuals, with plans to expand its employee base in the fourth quarter 2006.

Medgenics is managed by a team of individuals with decades of experience in biotechnology and biomedical devices, together with professionals from the healthcare, finance, medical, and academic communities. The Board of Directors includes current and former directors of international healthcare companies, and the Scientific Advisory Board (SAB) includes past presidents of the Renal Physicians Association, the American Gastroenterological Association, and the American Society of Gene Therapy. Biographies of these individuals are provided on pages 10-13.

Dr. Pearlman raised $17 million in funding in four equity rounds, raised an additional $1 million in Israeli government funding, and took the Company through its first clinical trial. In late 2003, there was a change of management, and under the leadership of the alternate CEO, the Company failed to raise additional funds. With dwindling remaining reserves, operations were brought to a halt in the third quarter 2004. Medgenics relaunched operations with the return of Dr. Pearlman as the CEO and raised initial restart funding of $1 million from private investors in the first quarter 2006. By May 1, 2006, the Company had completely reorganized, recapitalized, and resumed its development activities with a small, focused team. Since restart, the Company has developed the first versions of its sustained-action Biopumps intended to treat anemia and chronic hepatitis C.
Growth Strategy

Medgenics’ corporate growth strategy incorporates a succession of events, as summarized below.

- Medgenics aims to complete preparations to start the Phase I/II clinical efficacy trial for EPODURE in the fourth quarter 2007, and likewise for INFRADURE in the first quarter 2008. To maintain this schedule, the Company plans to raise additional capital in first quarter 2007.

- The Company believes the advantages of its technology could attract strategic partners that would help its products enter and capture market share, and accordingly, is exploring opportunities with appropriate partners. Alternatively, Medgenics could implement a stand-alone strategy for self-promoting the Biopump technology in appropriate markets.

- Medgenics expects to have data from the EPODURE clinical trial within six months of its commencement; this could lead to its first partnering deal.

Raising Funds

In order to fund the completion of preparations for the clinical trials of its sustained-action Biopump platform technology, Medgenics aims to raise additional funds in first quarter 2007. These funds are intended to drive completion of preclinical preparations to start the EPODURE and INFRADURE efficacy trials, as well as to bring the device prototypes up to preproduction performance (enabling multi-center clinical trials). Alternatives for raising these funds may include a private or public offering.

Efficacy Trials

Currently, Medgenics is in the second segment of its timeline illustrated in Figure 3: testing its products in mice and planning to conduct clinical trials in humans. Having already completed a successful Phase I clinical trial of the short-action Biopump in humans for anemia, the Company is now testing its new sustained-action Biopump via extended in vitro laboratory testing and in vivo SCID mice testing. The extended in vitro data demonstrates that each sustained-action Biopump produces therapeutic quantities of protein for over five months, and the mice experiments to date show that the protein produced by Biopumps implanted in the mice is active for several months on a sustained basis. Therefore, based on the data obtained in the laboratory and in mice, the Company’s Scientific Advisory Board (SAB), pages 12-13, has recommended that the Company begin preparations for Phase I/II approval.

Figure 3
Medgenics Inc.
OPERATIONAL MILESTONES

Source: Medgenics Inc.
Part of the preclinical preparations include the cGMP manufacturing of the vector, now under regulatory review, that is to be used to deliver EPO or IFN-α genes into the Biopump. Two cGMP facilities have already provided quotations for the production contract. The mouse in vivo data has demonstrated that the Biopump protein therapeutic can be active on a sustained basis. Thus, the Company has begun preparations for Phase I/II approval.

Assuming the Company can raise funding according to the scheduled timeline, as depicted in Figure 3 (page 7), it could be ready to begin the efficacy trial for EPODURE by the fourth quarter 2007, and the INFRADURE trial would be ready to commence within a few months thereafter.

Assuming the Company can raise funding according to this schedule, it should be ready to begin the efficacy trial for EPODURE by the fourth quarter 2007, and the INFRADURE trial would be ready to commence within a few months thereafter.

Marketing Strategy

In 2005, patients received more than $11 billion of EPO injections to treat anemia. Patients treated with IFN-α for hepatitis C and some forms of cancer received $3.5 billion in IFN-α injections in 2005. Medgenics plans to compete in each of these markets either through strategic partnerships or through a stand-alone strategy to develop and produce the Biopump and provide protein therapy.

Strategic Partnerships

Medgenics’ platform technology gives the Company a number of potential opportunities to foster strategic partnerships for different proteins in a variety of clinical indications. Continued positive data could make the Company an attractive partner and support its plan to enter into separate agreements for its various products: EPODURE anemia treatment, INFRADURE hepatitis C treatment, and potential future products. Medgenics seeks to combine the benefits of not having to build a protein manufacturing plant with its technology’s therapeutic and cost advantages, in order to attract multiple partnering opportunities for the products in its pipeline. The Company seeks to enter into its first strategic partnership within the next 18-24 months. A benchmark for such a partnership is the licensing agreement between Human Genome Sciences Inc.’s (HGSI-NASDAQ) and Novartis AG (NVS-NYSE) announced in May 2006 for Albuferon (a slightly improved version of interferon-alpha) in which fees and payments to Human Genome Sciences could total up to $507.5 million.

Stand-Alone Strategy

Alternatively, Medgenics may employ a stand-alone strategy in which its entire Biopump platform technology is used to provide sustained protein therapy via a network of Biopump treatment centers.
Medgenics’ technology is protected by 48 patents and patent applications in the U.S. and worldwide. This includes one issued U.S. patent, nine pending U.S. patent applications, one issued foreign patent, and 37 pending foreign patent applications. The Company’s intellectual property (IP) portfolio covers the various elements of the Biopump platform technology—from tissue engineering to device implementation and systematic use in treating disease. Medgenics’ proprietary micro-organs (MOs), genetically modified MOs (Biopumps), Biopump EPO, Biopump production, processing, implantation, and the tools designed for use in the Biopump procedure are all included in the Company’s intellectual property portfolio. Medgenics currently licenses the rights to the MO and Biopump from the Hebrew University, Jerusalem. Table 1 provides a select snapshot of Medgenics’ issued and pending intellectual property portfolio.

### Table 1

**Medgenics Inc.**  
**INTELLECTUAL PROPERTY**

<table>
<thead>
<tr>
<th>Patent Name</th>
<th>Patent Number</th>
<th>Issued</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>In vitro</em> micro-organs</td>
<td>US 5888720</td>
<td>March 30, 1999</td>
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<table>
<thead>
<tr>
<th>Patent Name</th>
<th>Publication Number</th>
<th>Publication Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dermal micro-organs, methods and apparatuses for producing and using the same</td>
<td>WO 2004/099363</td>
<td>November 18, 2004</td>
</tr>
<tr>
<td>Device and methods for harvesting tissue samples of known geometry</td>
<td>WO 2003/049783</td>
<td>June 19, 2003</td>
</tr>
</tbody>
</table>

Medgenics has an experienced management team, Board of Directors, and Scientific Advisory Board (SAB), as well as regulatory affairs advisors. The Company’s leadership includes individuals with experience within the healthcare, finance, medical, and academic communities.

Management

Table 2 summarizes key individuals within management, followed by biographies.

<table>
<thead>
<tr>
<th>Name</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>Andrew L. Pearlman, Ph.D.</td>
<td>Chief Executive Officer, President, and Director</td>
</tr>
<tr>
<td>Baruch S. Stern, Ph.D.</td>
<td>Director, Bioscience</td>
</tr>
<tr>
<td>Phyllis K. Bellin, MBA</td>
<td>Director, Finance and Administration</td>
</tr>
</tbody>
</table>

Source: Medgenics Inc.

Andrew L. Pearlman, Ph.D., Chief Executive Officer, President, and Director

Dr. Andrew Pearlman is the founder and CEO of Medgenics and has raised $18 million for the Company to date. Since moving to Israel in 1981, Dr. Pearlman has over 25 years experience founding and managing biotechnology and medical device companies, as well as inventing and developing biomedical technology. Prior to founding Medgenics, Dr. Pearlman founded and served as CEO and chief scientist for TransScan R&D Ltd. (now Mirabel Medical Systems), where he raised $16 million and under whose leadership the company’s product, the T-Scan 2000 breast impedance scanner, was the first new medical imaging method for cancer detection to receive U.S. Food and Drug Administration (FDA) premarket approval in over 20 years. He has also founded or co-founded several other companies in the fields of diagnosis and patient monitoring. Dr. Pearlman holds a Ph.D. in biophysics from the University of California, Berkeley, where he completed his doctoral thesis under Nobel Laureates, Professors Melvin Calvin and Donald Glaser.

Baruch S. Stern, Ph.D., Director, Bioscience

Dr. Baruch Stern received a Ph.D. in molecular biology and biotechnology from Tel Aviv University in 1994, and thereafter completed a post-doctoral fellowship at the National Institutes of Health (NIH). Since then, Dr. Stern has garnered extensive academic and industry experience in cell and tissue engineering, as well as in a wide range of applied molecular and cellular biology technologies. From 2001 to 2004, he was development group leader of the molecular biology section at Medgenics, where he spearheaded tissue engineering and development of Biopump technology, including viral vector and assay development. Dr. Stern was also instrumental in creating and implementing cGMP production and standard operating procedures for the Phase I clinical study, as well as developing the Company’s skin harvesting, handling, and implantation devices. From 2004 to before Medgenics’ restart in 2006, he served as tissue engineering project manager at ProChon Biotech, Ltd., a company developing solutions to damaged cartilage.

Phyllis K. Bellin, MBA, Director, Finance and Administration

Ms. Phyllis Bellin received an MBA from Columbia University and was a corporate lending officer for Citibank (member of Citigroup Inc. [C-NYSE]), prior to coming to Israel in 1980. Since 1980, Ms. Bellin has managed finance and administration for several early stage, high-tech ventures in Israel. Most recently, she was a founder and vice president, finance and administration for Gintec Active Safety Ltd. and RoadEye Ltd., where she established and managed finance, human resources, and logistics for a group of early stage, high-tech companies in the automotive market. Ms. Bellin’s responsibilities included business planning, budgets, financial reporting, cost accounting, and implementing enterprise resource

Source: Medgenics Inc.
planning systems, as well as managing relationships with banks, accountants, suppliers, and government organizations, including Israeli Chief Scientist, Israel Investment Center, and European Union Fifth Framework program and investors.

**Board of Directors**

Table 3 summarizes the Company's Board of Directors, followed by biographies.

<table>
<thead>
<tr>
<th>Name</th>
<th>Position</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eugene A. Bauer, M.D.</td>
<td>Chairman of the Board of Directors</td>
</tr>
<tr>
<td>Andrew L. Pearlman, Ph.D.</td>
<td>Chief Executive Officer, President, and Director</td>
</tr>
<tr>
<td>Joel E. Kanter</td>
<td>Director</td>
</tr>
<tr>
<td>Stephen D. McMurray, M.D.</td>
<td>Director</td>
</tr>
<tr>
<td>Gary A. Brukardt</td>
<td>Director</td>
</tr>
</tbody>
</table>

*Source: Medgenics Inc.*

**Eugene A. Bauer, M.D., Chairman of the Board of Directors**

Dr. Eugene Bauer has been a member of Medgenics' Board since 2001. He is a Lucy Becker professor, Emeritus, in the School of Medicine at Stanford University. Dr. Bauer served as Dean of the Stanford University School of Medicine from 1995-2001 and as Chair of the Department of Dermatology at the Stanford University School of Medicine from 1988-1995. He is also a co-founder and emeritus member of the Board of Directors of Connetics Corporation (CNCT-NASDAQ), a publicly traded, dermatology-focused therapeutics company. He serves as director of Protalex, Inc. (PRTX-OTC.BB) and Peplin Biotech, Ltd. Dr. Bauer has been a NIH-funded investigator for 25 years, has served on review groups for the NIH, and has served as a member of the Board of Scientific Counselors of the National Cancer Institute (NCI) and the Advisory Council for the National Institute of Arthritis and Musculoskeletal and Skin Diseases. Dr. Bauer is also a member of the Institute of Medicine of the National Academy of Sciences. Dr. Bauer received an M.D. from Northwestern University.

**Andrew L. Pearlman, Ph.D., Chief Executive Officer, President, and Director**

Biography on page 10.

**Joel E. Kanter, Director**

Mr. Joel Kanter has been a member of Medgenics' Board since the Company's inception. Since 1986, Mr. Kanter has served as president of Windy City, Inc., a privately held investment company specializing in early stage venture capital. He is also the president and a director of Echo Healthcare Acquisition Corp. (EHHA.0B-OTC.BB), a blank check healthcare acquisition company. From 1993 through 1999, Mr. Kanter was a director and president of Walnut Financial Services, Inc., a venture capital and financial services firm. He currently serves as a director of I-Flow Corporation (IFLO-NASDAQ), Nesco Industries, Inc. (NESK.PK), Encore Medical Corp. (ENMC-NASDAQ), and Magna-Lab, Inc. (MAGLA.0B-OTC.BB)—all publicly held companies within the healthcare sector. Mr. Kanter is also a director of several private companies, including Modigene, Inc. and BioHorizons Implant Systems, Inc. Mr. Kanter earned a B.A. from Tulane University.

**Stephen D. McMurray, M.D., Director**

Dr. Stephen McMurray was one of the founders of Renal Care Group, Inc. (RCI-NYSE), a company that provides acute dialysis services. He served on the Board at Renal Care Group until their acquisition by Fresenius Medical Care AG & Co. (FMCAG [FMS-NYSE]) in March 2006. He is a past member of the Renal Physicians Association Board and has served on the Network Medical Review Board for many years. Dr. McMurray is very active in developing processes to improve patient care and outcomes, and is currently the medical director of the Fresenius Medical Care Health Plan. Dr. McMurray received an M.D.
from Indiana University Medical School in 1972, followed by medicine residency and nephrology fellowship at Indiana University Medical Center. He has practiced nephrology in Fort Wayne, Indiana, since 1977. He is a member of Indiana Medical Associates, a 45-member multi-specialty group and is past president of their Board.

Gary A. Brukardt, Director

Mr. Gary Brukardt has over 30 years of experience in the healthcare industry. From 2003 through March 2006, he was president and CEO of Renal Care Group. Mr. Brukardt led Renal Care Group’s acquisition by Fresenius Medical Care in March 2006, which resulted in the creation of the largest provider of dialysis services in the U.S. After the close of the transaction, Mr. Brukardt held the position of vice chairman, Fresenius Medical Care North America and CEO, Global Disease Management/Ambulatory Services until September 2006. He is currently serving as a consultant to FMCAG globally. Mr. Brukardt was executive vice president and COO of Renal Care Group from 1996 to 2003. From 1991 to 1996, he was executive vice president of Baptist Health Care Affiliates, a company that provides occupational medical centers/programs, urgent care, home healthcare, managed care, corporate health services, management of hospitals and hospital joint ventures, and an ambulatory surgery center. From 1991 to 1996, he was chairman of HealthNet Management, Inc., a managed care company.

Scientific Advisory Board

The Company is advised by a highly experienced and focused Scientific Advisory Board. Table 4 lists the members of this Board, followed by biographies.

<table>
<thead>
<tr>
<th>Name</th>
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<tr>
<td>Eugene A. Bauer, M.D.</td>
<td>Member</td>
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<td>Eithan Galun, M.D.</td>
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<td>Michael Hensley, M.D.</td>
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<td>Emmet B. Keeffe, M.D., M.A.C.P.</td>
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<td>Stephen D. McMurray, M.D.</td>
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<td>Allen R. Nissenson, M.D.</td>
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<td>Amos Panet, Ph.D.</td>
<td>Member</td>
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<tr>
<td>Mark Kay, M.D.</td>
<td>Member</td>
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Source: Medgenics Inc.

Eugene A. Bauer, M.D.

Biography on page 11.

Eithan Galun, M.D.

Dr. Eithan Galun is an associate professor of medicine at the Hadassah School of Medicine, Hebrew University, Jerusalem, and is director of the Gene Therapy Institute.

Michael Hensley, M.D.

Dr. Michael Hensley is a former U.S. Food and Drug Administration (FDA) medical officer and has served as senior regulatory affairs advisor and manager for numerous pharmaceutical and biotechnology companies. He advises Medgenics on its total product concept.

Emmet B. Keeffe, M.D., M.A.C.P.

Dr. Emmet Keeffe is professor of medicine and chief of hepatology at the Stanford University School of Medicine. He is a past president of the American Gastroenterological Association and a leading authority on chronic hepatitis C.
Stephen D. McMurray, M.D.

Biography on page 11.

Allen R. Nissenson, M.D.

Dr. Allen Nissenson is professor of medicine and director of the Dialysis Program at University of California at Los Angeles (UCLA). Dr. Nissenson is the past president of the Renal Physicians Association, a world-renowned nephrologist, and a leader in kidney medicine and EPO development. He also advises Amgen Inc. (AMGN-NASDAQ) and Baxter International Inc. (BAX-NYSE).

Amos Panet, Ph.D.

Dr. Amos Panet is professor of virology at the Hadassah School of Medicine, Hebrew University, Jerusalem, the former chief scientific officer of Biotechnology General, and a co-inventor of the Biopump technology.

Mark Kay, M.D.

Dr. Mark Kay is the past president of the American Society of Gene Therapy. He is also a professor of pediatrics and genetics at Stanford University.

Regulatory Affairs Advisors

In addition to the Scientific Advisory Board, Medgenics is closely advised by highly experienced experts in other key areas, particularly regulatory affairs. These individual’s biographies are provided below.

Michael Hensley, M.D.

Biography on page 12.

Andra E. Miller, Ph.D.

Dr. Andra Miller is a former expert microbiologist and gene therapy group leader at the FDA’s Center for Biologics Evaluation and Research (CBER)’s Cellular and Gene Therapies Division and is now a leading consultant in regulatory affairs for Medgenics. Dr. Miller has provided key guidance to the Company’s regulatory and clinical planning, assisting in the Company’s coordination with the FDA and in the approval of its clinical protocols.
Core Story

Medgenics Inc. ("Medgenics" or "the Company") is a closely held biopharmaceutical company developing a sustained-action protein therapeutic technology for the treatment of a range of diseases. As an alternative to bolus injections of proteins mass produced in animal cells (predominantly rodent cells), the Company is creating a biological pump, the Biopump, which works inside the patient's body to produce and deliver the active protein steadily and for a sustained duration to treat a targeted indication.

Medgenics has demonstrated proof-of-principle of its short-action Biopump version (capable of lasting 14 days). In a published Phase I clinical trial, the Biopump successfully produced and delivered erythropoietin (EPO) to patients suffering from anemia. The Company has now developed and confirmed the performance in laboratory and in mice of its next-generation, sustained-action Biopumps (capable of lasting four to six months) for both EPO and interferon-alpha (IFN-α) in treating anemia and hepatitis C, respectively. Medgenics believes that its platform technology can yield a pipeline of sustained-action protein drugs capable of offering treatment for a range of illnesses/conditions, including interferon-beta (IFN-β) for multiple sclerosis (MS), Factor VIII for hemophilia, and human growth hormone (hGH) for both stunted growth in children and slowing muscle atrophy in the elderly.

The Company is initially focused on treating anemia with its sustained-action formulation of EPO and hepatitis C with its sustained-action formulation of IFN-α.

Market Opportunity

The protein therapeutic market was valued at over $51 billion in 2005 and is forecast to reach $87 billion by 2010, according to Kalorama Information, due to heavy demand and rapid sales in the U.S. and Europe. In 2005, patients received more than $11 billion worth of EPO injections to treat anemia, and patients treated for hepatitis C and some cancers received $3.5 billion worth of injected IFN-α. Medgenics plans to target each of these markets either through strategic partnerships or by establishing a stand-alone strategy to develop and produce the Biopump, with the ultimate goal of providing superior protein therapy.

Currently, there is a need for technology that can smoothly deliver necessary proteins on a long-term basis and in a natural fashion while avoiding severe side effects. Examples of conditions that could benefit from a sustained-action Biopump platform technology beyond anemia and hepatitis C could include central nervous system disease, acquired immune deficiency syndrome (AIDS), cancer, chronic pain, hemophilia, and obesity. The Biopump technology also holds further promise for applications where treatment by injection is not practical or where cost-effective protein production is not feasible.

Source: Medgenics Inc.
Therapeutic Protein Technology

Figure 4 (page 14) provides an illustration of the current protein production and therapy process. When a therapeutic protein is ready for commercialization, companies must establish a plant to mass produce the recombinant protein in animal cells (predominantly rodent cells). These plants typically cost between $500 million to $1 billion and could take years to achieve current Good Manufacturing Practices (cGMP) approval. Once reliable production, purification, and formulation is achieved, the protein is delivered to local clinical sites where it can be injected into patients.

Bolus Injections

Recombinant proteins typically have a short half-life. For example, the half-life of currently injected EPO versions ranges from approximately 8 to 25 hours. Typically, after 24 to 48 hours, the injected protein’s concentration in the bloodstream has decreased to a point below an effective therapeutic level. In essence, the patient is without treatment until the next injection. Due to the therapeutic protein’s short half-life, a large bolus injection delivers a temporary overdose in an effort to increase treatment duration per injection. Typically, injections need to be administered every few days (3 to 10) for many months or years.

In Figure 5, the dashed line on the top and bottom outlines the therapeutic window—the desired range of protein concentration in the patient’s blood in order to provide effective treatment. The majority of the protein in a bolus injection is absorbed into the body all at once, resulting in initial concentrations far above the desired maximum.

The “bolus injection” line represents the protein concentration in the patient’s blood from time of injection to time of dissipation. Mild to severe side effects are likely to occur when protein levels are above the therapeutic window maximum. The protein level is typically within the therapeutic window for less than 24 hours. As it drops below the desired minimum, there is no longer any significant clinical effect, and the protein becomes ineffective in treating the disease. For this reason, injections are repeated two to three times per week. This process wastes costly protein with each bolus injection, has a significant likelihood of adverse side effects, provides therapy only for a fraction of the time (even if a patient never misses an injection appointment), and is only a short-term remedy.

PEGylation

Longer protein therapies using PEGylation—a process intended to lengthen the time a substance remains in the bloodstream without being metabolized and excreted by the body—still require injections at least every one to two weeks. Injecting larger protein doses can extend the life of the treatment such as IFN-α, but the large concentrations can often cause adverse side effects, such as flu-like symptoms including fever, chills, headache, muscle and joint aches, and a rapid heartbeat.

Source: Medgenics Inc.
MEDGENICS’ BIOPUMP PLATFORM TECHNOLOGY

Medgenics’ Biopump platform technology is an innovative technology that converts an excised sample of the patient’s own dermal tissue into an internal protein production plant through *ex vivo* transduction with a viral or non-viral vector and re-implantation of the tissue. The technology is designed to deliver natural therapeutic proteins, on a sustained basis, without the overshoot and undershoot associated with injection, as described on page 15 (and in Figure 5). Medgenics’ unique method for production and delivery of therapeutic proteins differentiates it from competitors in the protein therapeutic market. Having already developed and demonstrated proof-of-principle for its Biopump platform technology, the Company believes that its advantages could enable it to gain access to this market and position Medgenics to become a key participant in the space. The Company’s Biopump platform technology (Harvester, Implanter, Ablator, and Bioreactor), illustrated in Figure 6, is described step-by-step by corresponding letter below.

The Procedure

**Figure 6**
Medgenics Inc.
THE BIOPUMP TECHNOLOGY PROCEDURE

- **Letter A.** A proprietary vacuum-activated jig and high-speed biopsy instrument, called the DermaVac, is used to extract a small piece of tissue from the skin’s lower level, the dermis. The vacuum-activated jig positions the skin and guides a hollow core needle, providing straight-forward removal of the tissue. This procedure can be performed with a local anesthetic in a physician’s office and provides rapid healing with no appreciable scars.

- **Letter B.** After harvesting, the dermal tissues (micro-organs [MOs], detailed on page 17) are transferred to a processing station, the Biopump Bioreactor. The MOs are then injected into the left side of the cassette on the Bioreactor.

- **Letters C and D.** While in processing, the MO is transduced (it receives a transfer of genes into a cell) with a viral vector that has been engineered to contain the gene necessary for secretion of a select protein (Letters C [viral vector] and D [transduction process]). Medgenics is also investigating whether nonviral vectors can be effective as alternatives to viral vectors for transducing MOs.

- **Letter E.** After transduction, the dermal tissue becomes a biological pump, expressing the desired protein at a defined number of micrograms per day.

*Source: Medgenics Inc.*
- **Letter F.** Protein secretion levels are measured to identify the optimal number of sustained-action Biopumps needed for treatment of the patient's ailment.

- **Letter G.** Prior to reinsertion, the Biopumps are washed to remove the remaining viral vector.

- **Letters H and I.** Approximately 10 days after harvesting, the modified tissue—now a Biopump—is implanted back into the patient, where it functions as normal tissue (Letter H), continuously producing and delivering the protein to the body (Letter I).

**Key Components for Procedure**

**Micro-Organ**

The extracted dermal tissue is referred to as a micro-organ (MO), a term originally coined at the Hebrew University in Jerusalem and further developed by Medgenics to encompass harvested human dermal tissue. After transduction with the viral vector, the MO becomes a Biopump expressing the therapeutic gene which produces the desired therapeutic protein. The MO must have two characteristics: (1) it must maintain the natural structure of the portion of the skin removed, and (2) the dimensions of it must be carefully controlled. When the MO has the appropriate geometry and maintains the same structure outside the body as it does inside, it can continue to function as viable tissue, producing the protein post-transduction long past the 10 days that it is kept *ex vivo* in practice. Controlling the dimensions of the MO enables nutrients to reach all the cells through passive diffusion and ensures that the sufficient amount and types of cells in their normal architecture are present to enable normal tissue function. Medgenics' DermaVac—its MO harvesting technology—reproducibly and reliably extracts an MO from a patient's skin. The typical MO is 2-3 mm in diameter and 30-40 mm in length. Figure 7 compares the size of the MO to that of a toothpick.

**Bioreactor**

Medgenics has completed initial proof-of-feasibility of its Biopump Bioreactor, which was developed during the Phase I clinical trial. Illustrated in Figure 8, its single-use cassette can hold eight MOs, representing one sealed cassette per patient. Laboratory tests showed that the device can produce eight functionally equivalent Biopumps simultaneously. However, further improved processing methods and ongoing development of Biopump processing are reducing the number of Biopumps needed to treat a patient.

For example, based on the results of Medgenics' previous proof-of-principle clinical trial, together with the protein production levels of typical sustained-action Biopumps, administration of two or three sustained-action EPO Biopumps (such as EPODURE) are likely to be sufficient to treat a typical anemic patient. Likewise, one to three sustained-action IFN-α Biopumps should be adequate to treat a typical hepatitis C patient. Medgenics believes that with a reasonable engineering effort, the Company can complete development of a reliable, automated, cost-effective system that can be used in hospitals and clinics worldwide.

**Viral Vector**

The viral vector is a deactivated virus that has been genetically engineered to bear the gene that codes the MO for the desired protein. The virus can not reproduce but can only invade the cells to which it is exposed. It is then broken down in those cells. When the vector is exposed to the MO, the virus enters the cells of the MO and brings the gene into the cell nucleus. Once inside the nucleus, the gene uses the
ordinary protein expression machinery within the cell to express the gene, causing the cell to produce the protein. That protein is then secreted from the cells of the MO, making it a "Biopump."

A significant drawback with the use of most viral vectors for human applications is the fact that the human immune system recognizes these entities and attacks them. This is commonly referred to as immunogenicity. For example, since most of the world’s population has been exposed to adeno virus (the common cause of stomach flu), it is natural that the general population has antibodies against the virus and any further exposure to the adeno viral proteins causes an immunogenic reaction. Since Medgenics’ first clinical study used a “first-generation” adeno viral vector, which contained a substantial number of viral genes in addition to the gene for EPO, the cells which absorbed the vector produced not only EPO but also viral proteins, thus drawing an immune response towards those cells.

To enable a sustained-action Biopump, immunogenicity must be avoided and a different kind of vector must be used—one which neither introduces viral proteins into the tissue nor continues to produce viral proteins when it is in the body. In developing its sustained-action Biopump, Medgenics has drawn upon recent significant advances in adeno viral technology from major research centers, which could effectively prevent the immunogenicity problem, by incorporating the following:

- Using a “gutless” adeno virus (a vector containing no viral genes, thus preventing it from producing viral proteins); and
- Washing the Biopumps during several days of ex vivo processing in order to reduce the number of free vectors to near zero and allow remaining viral proteins to be metabolized. This action reduces the transfer of any viral proteins to the patient to near zero.

The successful combination of the “gutless” adeno virus technology with the unique properties of the MO led to the creation of Medgenics’ sustained-action Biopumps, which could be a key advancement for the delivery of protein therapy.

**Biopump Termination and Dose Reduction**

Should the Biopump’s protein dose in the body need to be reduced, or ceased altogether, Medgenics has safe and effective methods to completely halt the function of one or more implanted Biopumps through the use of ablation. For example, if a patient has received four Biopumps but needs to reduce the dose by 25%, this can be done by ablating one of the Biopumps. The Company has shown three ways to ablate the Biopump: laser, radiofrequency (RF) needle, and surgical removal. The RF needle is an electric needle, such as those commonly used in microsurgery. These clinically accepted methods have been tested on Biopumps in pigs and mice, but were not needed in the Phase I human clinical trial.

Importantly, the capability to locate the Biopump under the skin and stop its production of protein differentiates Medgenics from other protein therapy technologies. The Company expects to further develop these methods of dose adjustment or termination in the coming year.

**CLINICAL TRIALS**

**Preclinical Research Results**

In laboratory tests with the short-action Biopump, Medgenics researchers proved that the Biopump provided dose-dependent delivery of active protein into the blood of Severe Combined Immunodeficient (SCID) mice, showing a direct correlation of the pre-implantation in vitro secretion levels with the post-implantation serum levels in the mice. Tests in the SCID mice also proved that the sustained-action Biopump could provide a dose-dependent delivery of active protein as well, and that the treatment could be reversed. Medgenics researchers were able to ablate the MO with either an RF needle or surgical removal, causing cessation of protein delivery.

Details of the Company’s preclinical investigations and its past Phase I clinical trial have been published in *Molecular Therapy*, a journal by the American Society of Gene Therapy, and in *Blood, The Journal of the American Society of Hematology*, respectively.
Phase I Clinical Trial for Short-Action Biopump EPO in Anemic Patients

Procedure

The Phase I trial harvested dermal tissue from under the abdominal skin of 13 patients—all of whom were previously diagnosed with stage III and IV chronic kidney disease (CKD). Stage III and IV CKD patients suffer from moderate to severe levels of decreased kidney function. The dermis MO tissue samples were removed in an ambulatory operating room using standard procedures and local anesthesia. At the cGMP cell processing facility at Hadassah-Hebrew University Hospital, the MOs were transduced with an adeno vector (first-generation and specifically designed to express human EPO [hEPO]) using manual cell culture techniques (the Bioreactor was under development at this stage), and the Biopumps began producing hEPO. The secretion of hEPO from each Biopump was then measured to determine the proper patient dosage. Before reinsertion of the Biopumps into the patients, each Biopump was thoroughly washed to remove free adeno vector (approximately 0.06% remained as residual incorporated vector). The newly created Biopumps were implanted into the patients 9 to 10 days after the initial harvest. The number implanted per patient (ranging from one to seven Biopumps per patient) was dependent upon the previously measured hEPO secretion rate and patient weight. The Biopumps were injected directly under the skin approximately 2 cm apart.

No Side Effects

The patients’ healing processes were observed six to eight days after implantation, and a small incisional biopsy was taken from a Biopump in each patient 20 to 22 days after implantation. The healing process was documented again 9 to 11 days after the biopsy was taken. In addition, patients were observed at home during and after the study by a qualified nurse, and clinical examinations for adverse effects continued for six weeks after the study. At the end of this period, there were no significant drug-related adverse effects to the Biopump procedure. In fact, after two years of follow-up on these patients, Medgenics had not received news of any adverse reactions to their technology. A summary of the Phase I human clinical trial timeline and procedure is provided in Table 5.

Results

Medgenics’ first clinical trial of its short-action Biopump technology demonstrated proof-of-principle for the method of converting human dermal cores into mini protein production plants, as well as proved that implantation of these back into the same patients could safely and significantly increase the patient’s level of protein on a short-term basis. The expression period was only 14 days in this trial due to the anticipated immune response to the first-generation adeno vector. However, the Biopumps still managed to increase the short-term serum EPO levels above the baseline as well as increase the reticulocyte count in patients. Most patients’ EPO serum levels returned to baseline on day 10. The Biopump EPO proved that it could be dose-controlled, reproducible, and free of significant adverse effects, as well as capable of promoting patient compliance. Although short by design, this trial provided critical proof-of-principle data for the prototype devices used to harvest and implant the Biopump. Recent advances with a “gutless” adeno vector (referenced on pages 21-23) are expected to enable sustained-action Biopumps to provide at least four to six months of high level protein delivery.
Figure 9 illustrates the hEPO serum levels and reticulocyte counts in patients who received implants with the first-generation adeno vector Biopump. (A) presents the net rise in hEPO levels compared to the pre-implantation baseline for patients in the low-dose cohort; (B) presents the same measurements in the high-dose cohort; and (C) presents the efficacy measured by the reticulocyte count (new red blood cell production) of four patients from the high-dose cohort.

Developing Sustained-Action Biopump Technologies

Major advances have been recently reported in alternative versions of the adeno vector, as well as in other non-immunogenic vectors, that resolve the well-known immunogenicity problems of the first-generation adeno vectors. Figure 10 illustrates how the duration of protein expression in normal baboons increased from weeks with the first-generation adeno vector (similar to Medgenics’ first clinical study) to one to two years when the first vector was replaced with a fourth-generation adeno vector. The increase in expression indicates that this new vector appears to solve the immune rejection problem. Continuing the developments, scientists at the Baylor College of Medicine in Houston, Texas, have further developed a “gutless” adeno vector (or helper-dependent adeno vector [HDAd])—a vector containing no viral genes, thus prevented from producing the viral proteins that cause immune rejection. As shown in Figure 11, an injection of a large amount of the “gutless” adeno vector directly into the livers of normal baboons was found to produce one to two years of steady, high serum protein levels.

Similar results were also reported in experiments with dogs, where year-long production of Factor IX protein was used to treat hemophilia in the dogs. These experiments confirm the theory that a “gutless” adeno vector appears to solve the immune rejection problem of previous adeno vectors.

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**Figure 10**

Medgenics Inc.

COMPARISON OF EXPRESSION FROM THE FIRST-GENERATION ADENO VECTOR TO THE FOURTH-GENERATION ADENO VECTOR IN NORMAL BABOONS

![Graph showing expression comparison](source.png)


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**Figure 11**

Medgenics Inc.

SUSTAINED EXPRESSION WITH NEW “GUTLESS” ADENO VECTOR IN NORMAL BABOONS

![Graph showing sustained expression](source.png)

The next crucial step for Medgenics was to have versions of the “gutless” adeno vector prepared with the EPO and IFN-α genes, and test whether they can be used to turn human skin dermis MOs into Biopumps that produce therapeutic levels of protein for many months. Medgenics formed a collaboration with the Baylor College of Medicine for this purpose. As shown in Figure 12, after more than 135 days of in vitro testing at the Company, the new Biopumps created using the “gutless” adeno vector still provided a steady, high level EPO secretion rate.

Reviewing this data, the Company’s Scientific Advisory Board (SAB), and many gene therapy experts at a recent meeting of the American Society for Gene Therapy, stated that they believe the Biopump with the “gutless” adeno vector could provide at least six months of sustained protein delivery in patients (and possibly more). The data also show that, without any optimization (a tactic commonly used in the protein therapy industry to increase protein output), the level of EPO protein output from the new “gutless” adeno vector on day 10—when it would be implanted—was steady at approximately 500-600 units/day. Based on its previous clinical trial, the Company estimates that approximately 1500-2000 units/day (three to four non-optimized sustained-action Biopumps) are needed to effectively treat a 70 kg (approximately 155 lbs.) anemic patient. Thus, even non-optimized, these Biopumps already have sufficient production to enable treatment of a typical anemic patient with only a few Biopumps.

In addition, Medgenics has now demonstrated that the Biopump IFN-α utilizing the new “gutless” adeno vector also provides similar sustained protein production of IFN-α in vitro. The data presented in Figure 13 (page 23) illustrates the results from the first six weeks of testing using a Biopump IFN-α and Biopump EPO made from the same patient. The data show sustained, high-level, in vitro protein production of IFN-α and EPO.

To further increase protein output, Medgenics used a synthetically produced gene, which has an optimized gene sequence for EPO. Using an optimized or synthetic gene in the vector can produce longer lasting and higher levels of protein. Medgenics saw an increase in protein output of 50-100% at any given time with the optimized gene compared to the non-optimized gene. Likewise, Medgenics has also produced Biopumps using these vectors with optimized IFN-α. The Company continuously seeks to improve its technology, and is exploring and developing Biopumps using additional types of vectors, such as the adeno-associated virus (AAV) double stranded vector, and non-viral vectors. Medgenics believes that these other vectors could offer further advantages, particularly the future possibility of not having to use a virus at all.
Testing in Animal Model

Having shown that the sustained-action Biopump maintains therapeutic levels of protein production in vitro for many months, the next critical step for the Company was to demonstrate that implantation of the new Biopumps in appropriate animals causes months of sustained elevation of serum levels of the protein as well as the desired therapeutic effects. To permit the testing of human skin Biopumps that produce human protein, an animal model whose immune system will not reject the implanted Biopumps must be used. Medgenics has prior experience using an animal model—SCID mouse—that has been approved by regulatory agencies for this purpose.

Medgenics has now demonstrated in SCID mice models that the EPODURE Biopump can actively elevate the serum EPO and the mouse hematocrit for over 10 weeks. Extended elevation in the mouse hematocrit serves as proof that the EPODURE Biopump is active and viable in an in vivo system. Results from the SCID mice models are presented in Figure 14. The upper curve shows the raised hematocrit levels over the control group (lower curve). The control group received the human skin MO before it was transduced to become EPODURE; thus, it did not produce EPO in the mice. Likewise, implantation of INFRADURE in SCID mice resulted in elevated serum IFN-α levels for over three months.
MEDGENICS’ PROTEIN THERAPY

As described in the preceding section, Medgenics seeks to improve the current scenario of protein therapy by providing sustained-action protein therapy, where a single implantation can produce and deliver protein to the patient that is within the therapeutic window for at least four to six months. This technology could potentially eliminate side effects associated with bolus injections and could offer a convenient, lower-cost solution to patients requiring protein therapy.

Medgenics is using its sustained-action Biopump platform technology to focus initially on improving protein therapeutics for anemia and chronic hepatitis C. More detailed descriptions of these disorders are provided in the accompanying sections. The Company believes that the Biopump technology is likely to appeal not only to those who now receive protein therapy, but also to a larger population of patients who could benefit but are unwilling to suffer the unpleasant side effects currently associated with injections.

Disease Focus Areas

Anemia

The National Kidney Foundation’s Kidney Disease Outcomes Quality Initiative estimated that in the U.S. approximately 20 million people suffer from anemia as a result of chronic kidney disease (CKD). Additionally, the initiative estimated that as many as 67 million people in the U.S. with hypertension and diabetes are at an increased risk for CKD and subsequently anemia. Anemia occurs when a person does not have enough red blood cells (RBCs) or hemoglobin in them. RBCs, also known as erythrocytes, carry hemoglobin, a protein that delivers oxygen from the lungs throughout the body. When the number of RBCs decreases, the heart must work harder to deliver oxygen where it is needed throughout the body.

RBCs, produced in the bone marrow, are regulated by a hormone called erythropoietin (EPO). Normally, when the body’s oxygen level is decreased, it compensates by increasing its EPO production. EPO then stimulates the stem cells contained in the bone marrow to produce more RBCs and increase how quickly the RBCs mature. When this natural response is hindered through kidney disease or other causes, the body can become anemic. Approximately 90% of EPO is made in the kidneys.

There are various types of anemia, including iron deficiency anemia, vitamin deficiency (such as folate or vitamin B-12), anemia of chronic disease (e.g., Crohn’s disease, end-stage renal disease [ESRD]) or kidney failure, aplastic anemia, anemia associated with bone marrow disease (such as leukemia), hemolytic anemia, and sickle cell anemia. There are several other more rare forms of anemia, such as thalassemia and anemia caused by defective hemoglobin. Medgenics' technology aims to treat anemia of chronic disease.

The main symptom of most types of anemia is fatigue. Other signs and symptoms of anemia include weakness, pale skin, a fast heartbeat, shortness of breath, chest pain, dizziness, cognitive problems, numbness or coldness in the extremities, and headaches. Initially, anemia can be so mild it goes unnoticed; however, signs and symptoms increase as the condition evolves. If the anemia is severe enough, exhaustion and other symptoms may interfere with everyday tasks.

Although anemia is often treatable, it may take several weeks to months for RBC levels to return to normal after treatment. If untreated, anemia can lead to an arrhythmia or congestive heart failure (CHF) as the heart must pump more blood to compensate for the lack of oxygen in the blood. Untreated pernicious anemia can lead to nerve damage and decreased mental function since vitamin B-12 is important not only for healthy RBCs but also for optimal nerve and brain function. Some inherited anemia, such as sickle cell anemia, can be serious and lead to life-threatening complications. A large and significant blood loss in a short time period can also result in acute severe anemia and ultimately be fatal.

Current Treatment

Current treatment for chronic anemia is multiple and frequent subcutaneous injections of recombinant EPO, most often in the thigh or abdomen. The recombinant EPO is generally administered to patients via injection three times per week with Amgen’s EPOGEN® or once a week by Amgen’s Aranesp®. These products and others used to treat anemia are described in greater detail in the Competition section (pages 31-34). Some of the shortcomings of current anemia treatments that Medgenics seeks to address are bulleted on page 25.
Patient adherence. Any treatment that is based on the administration of serial injections as frequently as three times a week is subject to poor patient adherence, as the prescribed regimen can lead to inadequate treatment results. CKD patients are “pre-dialysis” (not connected to a dialysis machine), and therefore must visit the doctor’s office to receive EPO injections or self-inject at home. Both of these approaches can lead to non-adherence due to the inconvenience of coming into the office and reluctance by patients to self-administer an injection multiple times per week. In contrast, for patients with ESRD on hemodialysis, EPO is administered through the dialysis tubing or subcutaneously by the dialysis healthcare staff when the patient is in the clinic for the regular dialysis treatment. This eliminates the problem of non-adherence but involves considerable time and resources by the dialysis staff.

Poor clinical efficacy of bolus intravenous injection. Today, the majority of ESRD patients receive EPO intravenously as a bolus (high concentration) injection, which causes dramatic swings in serum EPO concentration from overshoot of many multiples above the maximum desired level to undershoot below the minimum effective level. The overshoot is considered necessary to optimize the response because with a short half-life of only 8.3 hours, EPO serum concentration using this approach will reach and remain within the desired minimum-to-maximum range for at least a day. However, the overshoot may contribute to high-risk side effects (such as hypertension and stroke due to clot formation) and is clearly inefficient, wasting EPO, while undershoot is also inefficient because inadequate stimulation of erythropoiesis (red blood cell formation) occurs. The result is difficulty in maintaining stable hemoglobin within a desired range, and frequent, inconvenient dose adjustments being required.

Increasing safety concerns about recombinant EPO. Certain manufactured recombinant EPO has recently been shown to cause pure red cell aplasia (PRCA), a serious and life-threatening condition where antibodies to EPO destroy the RBC precursor cells in the bone marrow. Patients with PRCA have severe anemia and require blood transfusions or potent immunosuppressive therapy to survive. Although the recent epidemic of PRCA has been associated with a manufacturing problem with one brand of EPO, it illustrates a vulnerability of recombinant proteins; small changes in manufacturing or handling can cause these generally safe proteins to become immunogenic—stimulating the body’s immune system in an undesirable way. Medgenics’ EPODURE is produced using the patient’s own tissues; therefore, it should have a substantially lower risk of causing PRCA than recombinant EPO.

High cost. Therapeutic proteins, such as EPO, are very costly to the end user, in part because the establishment of approved production of recombinant proteins is an inherently costly process (typically costing hundreds of millions of dollars and requiring several years) with high ongoing costs of production. Medicare spends more on various forms of EPO than on almost any other drug. Because of the high costs, Medicare and many commercial healthcare plans will usually only pay for the amount of EPO that partially corrects anemia. Many patients may benefit from more complete anemia correction, but this is not typically possible with the current payment constraints.

Side Effects

The necessity of injecting large concentrations of EPO into the body through bolus injections can trigger side effects, many of which are severe. Some of these are flu-like symptoms such as joint pains, weakness, dizziness, and fatigue, while others include headaches, high blood pressure, skin irritation, and skin rash. In addition, the recombinant EPO used in current anemia therapy can cause the formation of antibodies in the patient. In some cases, these antibodies are known to cause PRCA (described above). Past president of the Renal Physicians Association, Professor Allen R. Nissenson, M.D. (biography on page 13), believes the EPO produced by the patient’s own cells in EPODURE is much less likely to cause PRCA than commercial EPO produced by animal cells (predominantly rodent cells).

Hepatitis C

Hepatitis is an inflammation of the liver usually caused by viral infections, toxic agents, or drugs, but may also result from an autoimmune response. The only way to discover and diagnose hepatitis is through a variety of blood tests, such as liver function tests, which can give an indication of how much inflammation exists, as well as other tests to determine which virus is responsible. Hepatitis is described as acute if the condition resolves within six months, whereas it is described as chronic if the condition persists for longer than six months.
Statistics

Hepatitis C (formerly called non-A/non-B hepatitis) is caused by the hepatitis C virus (HCV). Worldwide, it is estimated that there are 170 million chronic carriers, and three to four million new infections each year. Approximately 75% to 85% of individuals infected with HCV will develop a chronic infection, of which approximately 15% to 20% will develop chronic liver disease progressing to cirrhosis. Between 1% and 5% of people with chronic infections will develop liver cancer over a period of 20 to 30 years.

An estimated four million people have been infected with HCV in the U.S., of whom 2.7 million are chronically infected. Chronic HCV infection is the leading cause of liver disease in the U.S. and many other western countries. According to the U.S. Center for Disease Control and Prevention (CDC), it is the most common chronic blood-borne infection in the U.S.; however, new infections in the U.S. have dropped to less than 25,000 in 2001 from approximately 240,000 annually in the 1980s. This is largely due to the availability of a diagnostic antibody test, which was introduced in 1990 to screen for and eliminate HCV-infected blood from the nation's blood supply.

Since 1990, all blood in the U.S. has been screened for the presence of the virus, thus eliminating almost all cases of transmission through transfusion. While this screening test has also been adopted by many other industrialized nations, the rest of the world is still at risk from transfusions as well as other common routes of transmission, especially contaminated needles. Without blood screening, many if not most carriers are not aware that they are infected or that they should be taking precautions against infecting others.

While the incidence of infection in the U.S. has decreased since the 1980s, the rate of deaths attributable to HCV continues to increase as people infected decades ago begin to succumb. According to the CDC, approximately 8,000 to 10,000 people currently die each year from HCV-related liver disease. The CDC has predicted that the death toll will triple by the year 2010 and exceed the number of U.S. deaths due to AIDS. In addition, HCV is now the most common blood-borne infection in the U.S., and is the most common reason for liver transplants. According to Hepatitis Central (http://hepatitis-central.com), over the next 10 to 20 years, chronic hepatitis C is predicted to become a major burden on the healthcare system as many patients who are currently asymptomatic will progress to end-stage liver disease and cancer.

Current Treatment

Current treatment for chronic hepatitis C consists of a combination of interferon injections and a ribavirin pill supplement. There are several varieties of interferon injections available (Roferon®-A, Intron® A, Infergen®, and Rebetron®) for patients with chronic hepatitis C. These injections are administered three times a week, although in some cases, they must be administered every other day. This combination is costly, may cause considerable side effects such as flu-like symptoms, depression, and reduction of white blood cell count, and is effective in only approximately 30% of selected patients.

A second type of treatment uses pegylated interferon proteins (PEG-INTRON® and Pegasys®). This treatment contains polyethylene glycol (PEG) to help the interferon stay in the patient’s body longer, and must be injected once a week. Treatment duration depends upon the genotype of the individual case of HCV infection. The goal of treatment is for a patient’s HCV RNA (viral load) to be undetectable 24 weeks after completion of treatment. This is called a sustained virologic response (SVR) and is equivalent to a probable cure. Patients infected with HCV genotype 1 require 48 weeks of treatment with either Pegasys® or PEG-INTRON® plus oral ribavirin for an optimal chance for a SVR, while patients with HCV genotype 2 or 3 require treatment for only 24 weeks.

Another form of treatment, the infusion pump system, can produce a steady and sustained delivery of IFN-α, thereby reducing side effects and in some ways validating the desirability of Medgenics’ approach. However, it is not a practical alternative to injections as this pump still requires use of the same costly animal-produced protein, which loses potency if carried at body temperature for days or weeks. In addition, this pump poses safety- and practicality-related challenges since patients must wear an external infusion pump system.
Side Effects

Standard hepatitis C treatment can have mild to severe side effects. These side effects can cause up to 40% of patients to reduce therapy dosages, and at least 20% of patients to discontinue treatment altogether. Early side effects that generally lessen with continued treatment include flu-like symptoms such as fever, chills, headache, muscle and joint aches, and a rapid heart rate. Fatigue, hair loss, low blood count, difficulty focusing, moodiness, and depression are all moderate-level side effects a patient may experience with continued therapy. Less than 2% of individuals suffer severe side effects such as thyroid disease, depression, suicidal thoughts, seizures, acute heart or kidney failure, eye or lung problems, hearing loss, blood infection, and rarely, death due to liver failure or blood infection. Liver disease may severely or fatally worsen with treatment.

The epidemic proportions of chronic hepatitis C, the limited efficacy and costly nature of approved therapeutics, the high cost of liver transplants (approximately $250,000 each), and the enormous burden on the healthcare system just in medical and work-loss costs, all call attention to the need for prophylactic vaccines as well as new therapies to treat the disease.

Medgenics’ Products

Medgenics is initially focused on developing two products based on its Biopump platform technology: EPODURE to treat anemia and INFRADURE to treat chronic hepatitis C.

Origin of Products

EPODURE and INFRADURE were first created when Medgenics split 40 MOs into two groups. The first group received the vector with the EPO gene (creating EPODURE) and the second group received the IFN-α gene (creating INFRADURE). By changing the gene, Medgenics changed which protein was expressed and still had a working Biopump. In this single move, the Company was able to demonstrate the key step towards a completely separate, second product, indicating the power of its platform technology.

EPODURE

EPODURE is Medgenics’ product in development to treat anemia, an estimated $11 billion market in the U.S., which is rapidly growing. EPODURE has been developed using sustained-action erythropoietin (EPO) and has applications for the treatment of dialysis, pre-end stage renal disease (pre-ESRD), AIDS therapy, oncology, and other areas where anemia impacts a patient’s health. In its Phase I proof-of-principle human clinical trial in anemic patients (described on pages 19-20), the short-term version of the Company’s technology proved safe, reliable, and demonstrated brief efficacy.

The positive response of patients in the trial indicated that a sustained-action Biopump could improve patient compliance since the procedure was well tolerated. Moreover, replacing frequent injections would provide for an improved quality of life. Through the use of natural protein sources—i.e. the patient’s own tissues—and avoiding both overdose and underdose, the sustained-action Biopump could promote increased safety and could significantly lower costs for payers and extend anemia management to undertreated populations.

INFRADURE

INFRADURE is Medgenics’ sustained-action interferon-alpha (IFN-α) to treat hepatitis C, a $3.5 billion market in the U.S. IFN-α has anti-viral properties that prevent the entry of a virus into a cell and limit the amount of new cells that can become infected. Interferon also inhibits the reproduction of viruses by interfering with the viral protein synthesis and preventing viral replication within the cell. The interferon family is currently used to treat a number of diseases, most prominently hepatitis C, but also cancer, hepatitis B, and Kaposi’s sarcoma as well.

INFRADURE builds upon EPODURE and the Biopump EPO technology. The IFN-α Biopump has been shown to produce several micrograms of protein a day for extended periods. Based on this, the Company believes that one or two sustained-action Biopumps may be sufficient to treat a typical hepatitis C patient without the side effects of frequent, inconvenient bolus injections.
Potential Applications of EPO and IFN-α Products

Table 6 summarizes some of the potential applications of Medgenics’ two primary products: EPODURE and INFRADURE. It also illustrates several of the other proteins that could benefit from the Company’s platform technology, particularly those that are off patent as of 2007.

<table>
<thead>
<tr>
<th>EPO Uses</th>
<th>Proteins</th>
<th>IFN-α Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia (all forms)</td>
<td>EPO</td>
<td>Hepatitis C</td>
</tr>
<tr>
<td>Dialysis</td>
<td>IFN-α</td>
<td>Oncology</td>
</tr>
<tr>
<td>pre-ESRD</td>
<td>IFN-β</td>
<td></td>
</tr>
<tr>
<td>AIDS</td>
<td>hGH</td>
<td></td>
</tr>
<tr>
<td>Oncology</td>
<td>G-CSF</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PDGF</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Factor VIII</td>
<td></td>
</tr>
</tbody>
</table>

Medgenics has also used the process of changing the gene (described under “Origin of Products” on page 27) to produce other proteins, such as the human growth hormone (hGH). hGH can be used for a variety of growth-related ailments, including promoting growth in stunted children or slowing muscle atrophy in the elderly or terminal cancer and AIDS patients. In addition, Medgenics’ technology could be applied to interferon-beta (IFN-β), another form of interferon used to treat multiple sclerosis (MS), as well as to granulocyte-colony stimulating factor (G-CSF), a growth factor encouraging the bone marrow to produce more white blood cells; platelet-derived growth factor (PDGF), which regulates cell growth and division; and Factor VIII, which can be used to treat uncontrolled bleeding in hemophilia. Medgenics believes that these are just a few of the treatments possible for the protein therapeutics market. Applications in other disease areas such as MS, cancer, obesity, wound healing, diabetes, arthritis, and chronic pain are also possible.

Technology and Product Benefits

Physician, Patient, and Payer Benefits

Medgenics believes that its technology can offer the equivalent of tens of thousands of dollars of reimbursed treatment at a considerably lower cost. In doing so, the Company’s therapy is likely to appeal to and offer benefits to doctors, patients, and third-party payers, as listed in Table 7 and described thereafter. The Company believes its technology can offer the following additional advantages:

- Eliminates frequent injections
- Reduces side effects
- Lowers costs
- Extends treatment to undertreated populations
- Increases efficacy
- Reversible treatment

Source: Medgenics Inc.
- **Reduces side effects.** Medgenics' therapy is expected to have fewer and less severe side effects associated with it than are associated with current recombinant protein production and delivery methods. The Company’s therapy does not use a bolus injection, thereby eliminating the health risks and side effects associated with overshoot. Bolus undershoots not only undertreat the patient’s illness, but could lead to conditions such as **neocytolysis** in EPO therapy. Efficient, continuous EPO dosing at optimal levels should eliminate this risk. It is believed that Medgenics' method will likely be safer since it produces protein from the patient’s own tissue instead of from animal cells (predominantly rodent cells). Recombinant proteins from non-human mammalian cells often have different **glycosylation** patterns from those of human cells, causing the formation of antibodies in some patients that can result in the onset of immune rejection, such as PRCA in EPO therapy. By contrast, producing protein from the patient's own cells is anticipated to reduce the risk of immune responses by reducing production of protein antibodies.

- **Lowers Cost.** The Biopump platform technology is expected to offer a cost-effective protein therapy. This procedure does not use a protein production plant, thereby eliminating the need for a $500 million to $1 billion-plus outlay to build the plant. The protein is continuously produced within the patient, eliminating the ongoing costs traditionally required to develop or purchase recombinant proteins such as hEPO.

- **Extends Treatment to Undertreated Populations.** The Company's technology is expected to extend treatment to undertreated populations. Patients who could not continue hepatitis C treatment because of the severe side effects are likely to be able to do so with THE sustained-action Biopump technology. In addition, third-party payers are often reluctant to pay for treatment until a condition is severe due to the cost considerations of injections; this could be remedied through Medgenics' cost-effective alternative therapy. Similarly, payers place upper limits on the amount of reimbursed protein injections. In EPO therapy, this limits hemoglobin levels, leaving many patients with continued anemia. Medgenics' therapy can return these decisions to the patients and their doctors. Additionally, the Company believes that the devices used in its Biopump procedure can be automated for practical and reliable implementation of Biopump therapy and placed in hospitals and clinics worldwide.

- **Increases Efficacy.** Continuous production and delivery of protein through a sustained-action Biopump is likely to increase efficacy. The sustained delivery of protein from the Biopump could provide greater reliability that effective dosages can be maintained in the patient versus an extended series of repeat bolus injections. Maintaining effective levels of protein within the therapeutic window in the patient optimizes efficiency and eliminates overshoot and undershoot.

- **Reversible Treatment.** The Biopump procedure is reversible. The MO can be ablated by laser, RF needle, or a surgical procedure, if necessary, as described on page 18 (Biopump Termination and Dose Reduction).

### Comparison to Current Protein Therapeutic Technologies

A summary of the difference between current drug delivery technologies and the Company’s Biopump platform technology is provided in Table 8.

<table>
<thead>
<tr>
<th>DELIVERY SYSTEM</th>
<th>MAJOR LIMITATION*</th>
<th>BIOPUMP THERAPY**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injections (IV, IM, SC)*</td>
<td>Inefficient bolus delivery, poor patient compliance, side effects of overshoot</td>
<td>Steady and continuous dose, patient-friendly, and convenient</td>
</tr>
<tr>
<td>Oral*</td>
<td>Digested in stomach</td>
<td>Delivered to circulation</td>
</tr>
<tr>
<td>Depot/Slow Release*</td>
<td>Small total capacity</td>
<td>Unlimited capacity</td>
</tr>
<tr>
<td>Inhalatory*</td>
<td>Small proteins only</td>
<td>All proteins</td>
</tr>
<tr>
<td>Transdermal*</td>
<td>Small proteins only</td>
<td>All proteins</td>
</tr>
</tbody>
</table>

*Requires protein manufactured in animal cells **Makes its own protein from patient's tissue

*Source: Medgenics Inc.*
A comparison between traditionally used gene therapy and the Company’s Biopump protein therapy is provided in Table 9.

<table>
<thead>
<tr>
<th></th>
<th>GENE THERAPY</th>
<th>BIOPUMP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose predictable</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Stays localized</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Reversible</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Adjustable dose</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Viral load</td>
<td>High</td>
<td>Low to none</td>
</tr>
<tr>
<td>Additional treatments</td>
<td>Not possible</td>
<td>Possible</td>
</tr>
</tbody>
</table>

Source: Medgenics Inc.
Competition

Medgenics possesses a unique technology with an unparalleled method for production and delivery of protein therapeutics. The Company faces competition within the field of protein therapeutics, directly from established competitors, which are using alternative protein manufacturing and different delivery methods for EPO and IFN-α to treat anemia and hepatitis C. In addition to EPO and IFN-α, many of these companies currently manufacture or are developing a wide array of proteins, such as G-CSF and hGH—areas Medgenics intends to target at some point in the future. Table 10 summarizes Medgenics’ primary competition, followed by brief descriptions of the products and product manufacturers. Following, in Table 11 (page 33), is a section of products which could one day compete with Medgenics and are in some stage of development.

Marketed Products

<table>
<thead>
<tr>
<th>COMPANY</th>
<th>PRODUCT NAME</th>
<th>APPLICATION</th>
<th>DOSAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amgen Inc.</td>
<td>Aranesp®</td>
<td>CRD anemia</td>
<td>weekly</td>
</tr>
<tr>
<td></td>
<td>EPOGEN®</td>
<td>ESRD anemia</td>
<td>3 times a week</td>
</tr>
<tr>
<td>Roche Holdings</td>
<td>Roferon-A®</td>
<td>HCV</td>
<td>3 times a week</td>
</tr>
<tr>
<td></td>
<td>Pegasys®</td>
<td>HCV</td>
<td>weekly</td>
</tr>
<tr>
<td></td>
<td>Copegus®, taken with</td>
<td>HCV</td>
<td>twice daily</td>
</tr>
<tr>
<td></td>
<td>Pegasys®</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schering Plough Corp.</td>
<td>PEG-INTRON®</td>
<td>HCV</td>
<td>weekly</td>
</tr>
<tr>
<td></td>
<td>REBETOL®, taken with</td>
<td>HCV</td>
<td>twice daily</td>
</tr>
<tr>
<td></td>
<td>PEG-INTRON®</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Intron®-A</td>
<td>HCV</td>
<td>3 times a week</td>
</tr>
<tr>
<td>Ortho Biotech Products, L.P.</td>
<td>Procrit®</td>
<td>anemia</td>
<td>3 times a week</td>
</tr>
<tr>
<td>(Johnson &amp; Johnson division)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Janssen Cilag</td>
<td>Eprex®</td>
<td>anemia</td>
<td>weekly</td>
</tr>
<tr>
<td>(Johnson &amp; Johnson division)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Source: Medgenics Inc. and Crystal Research Associates, LLC.

Amgen Inc.

Amgen Inc. has been a leading human therapeutics company in the biotechnology industry for 25 years. Pioneering the development of products based on advances in recombinant deoxyribonucleic acid (DNA) and molecular biology, the company launched the biotechnology industry’s first blockbuster medicines. Amgen’s product pipeline includes Aranesp® and EPOGEN®, injectable recombinant proteins manufactured for the treatment of chronic renal disease (CRD) anemia and end-stage renal disease (ESRD) anemia, respectively. Both products have FDA approval and are currently on the market. EPOGEN® is administered up to three times a week either during dialysis treatment or by a subcutaneous injection. Aranesp® has two weekly delivery methods—the Aranesp® SingleJect™ pre-filled syringe, which can be injected in a doctor’s office or at home and the pre-filled ‘SureClick™ autoinjectors for subcutaneous injection. In 2005, annual sales for Aranesp® were approximately $3.3 billion and sales for EPOGEN® were approximately $2.5 billion.
Roche Holdings

Roche Holdings (ROG.VX-VTX) has been active in the discovery, development, manufacture, and marketing of healthcare solutions for 100 years. The company’s focus is not only the diagnosis and treatment of manifest disease but also in offering ways of identifying and targeting diseases early, when their damaging effects can still be prevented. The FDA has approved three of the company’s primary products for the treatment of hepatitis C: Roferon-A®, Pegasys®, and Pegasys® with Copegus®. Roferon-A® is a recombinant protein injected subcutaneously three times a week for 12 months. Conversely, Pegasys® uses PEGylation to help the interferon last longer in the body and need only to be self-injected once a week for 24-48 weeks. Copegus® is an antiviral medication that can increase the efficacy of Pegasys® when taken together.

Schering Plough Corp.

Schering Plough Corp. (SGP-NYSE) is a global, science-based healthcare company striving to provide a steady flow of innovative, science-based medicines and services that improve the health of people around the world. Schering’s FDA-approved hepatitis C products are PEG-INTRON®, Intron®-A, and Rebetron®. PEG-INTRON® is a pegylated protein therapy injected once a week for one year. It can be self-injected with the PEG-INTRON REDIPEN® delivery system. PEG-INTRON® can be combined with REBETOL®, an antiviral drug, for a more effective combination treatment of chronic hepatitis C. Intron®-A is a recombinant protein that can be injected subcutaneously or intramuscularly and is to be taken three times a week for 18-24 months.

Johnson & Johnson

Johnson & Johnson (JNJ-NYSE) is a comprehensive manufacturer of global healthcare products, as well as a provider of related services for the consumer, pharmaceutical, and professional markets. Within the Johnson & Johnson family of companies are two companies, Ortho Biotech Products, L.P. and Janssen-Cilag, which manufacture protein therapies for anemia management. Ortho Biotech Products, L.P. is a biopharmaceutical company focused on products and services designed to enhance the lives of chronically ill individuals. Ortho Biotech was formed in 1990 and its products have treated over two million patients in the U.S. alone. Procrit®, the company’s injectable recombinant protein therapy, is designed to treat various types of anemia—from chemotherapy-related anemia and CKD patients to anemic patients undergoing elective, non-cardiac, non-vascular surgery. It can be injected intravenously or subcutaneously by a physician and should be administered three times a week. Janssen-Cilag develops and markets pharmaceutical products and services. Eprex® is the company’s EPO protein therapy for anemia associated with chemotherapy patients, patients with renal impairment, or patients undergoing orthopedic surgery involving considerable blood loss. Eprex® was approved for use in Europe in May 2006 and requires a weekly dosage.

Development Stage Products

Each of the products listed in Table 11 (page 33) and on the accompanying pages are being developed to target areas Medgenics is focusing on or intends to focus on in the future.

Human Genome Sciences Inc.

Human Genome Sciences Inc.’s mission is to discover, develop, manufacture, and market innovative drugs that serve patients with unmet medical needs, with a primary focus on protein and antibody drugs. The company was founded in 1992 and is based in Rockville, Maryland. Human Genome Sciences has entered into an agreement with Novartis AG to develop and commercialize Albuferon-Alpha™, a long-acting form of IFN-α for chronic hepatitis C treatment. Albuferon™ uses albumin fusion technology to fuse together the gene expressing human albumin with the gene expressing the active protein. Albuferon™ is currently in Phase II and is expected to enter Phase III prior to the end of 2006. Currently, the dosage requirements for Albuferon™ are estimated at one every two or four weeks.
Modigene Inc.

Modigene Inc. is a biopharmaceutical company working to develop longer lasting, proprietary versions of already approved therapeutic proteins. Modigene operates an R&D subsidiary located in the Weizmann Science Park, Nes-Ziona, Israel. The company’s technology attaches a naturally-occurring amino acid sequence, CTP, to therapeutic proteins in order to lengthen the protein’s lifespan in the body. This technology is still in the development stages. The company’s pipeline also includes MOD-701, a product that attaches CTP to EPO, and MOD-1001, which attaches CTP to G-CSF.

InterMune Inc.

InterMune Inc. (ITMN-NASDAQ) is a biotechnology company engaged in the research, development, and commercialization of therapies for pulmonology and hepatology. The company was founded in 1998 and is headquartered in Brisbane, California. With its partner, Array BioPharma Inc. (ARRY-NASDAQ), InterMune is working to develop a protease inhibitor compound, ITMN-191 (formerly ITMN B), for treatment of chronic hepatitis C. ITMN-191 is currently in the preclinical stage.

Nautilus Biotech

Nautilus Biotech was founded in January 2000 as a drug discovery company focused on the design and development of proprietary therapeutic proteins. One of Nautilus' leading products is Belerofon®, an IFN-α variant differentiated from native IFN-α by a single amino acid change that has been designed to increase resistance to proteolysis in the blood and intestine. This mutation is intended to allow Belerofon® to survive the intestine and reach the bloodstream, allowing the hepatitis C drug to be administered orally. Nautilus is expected to file an Investigational New Drug (IND) application for Belerofon® in 2006, and the drug could begin Phase I testing in the first quarter 2007. The company is using this same technology to develop an oral form of hGH, called Vitatropin™, which is currently in preclinical development.

Affymax Inc.

Affymax Inc. is a biopharmaceutical company specializing in synthetic peptide-based drugs for the treatment of kidney diseases and cancer. Affymax was formed in August 2001 as a spin-out from GlaxoSmithKline plc (GSK-NYSE). The company’s lead product is Hematide™, a synthetic peptide-based, erythropoiesis-stimulating agent for anemia from CKD and cancer. Hematide™ is in Phase II trials.
for CKD anemia and a Phase II dose-finding trial for patients with chemotherapy-related anemia. The company believes that Hematide™ has a novel amino acid sequence that is not likely to cause PRCA, and may include only a monthly administration.

**Vertex Pharmaceuticals Inc.**

Vertex Pharmaceuticals Inc. (VRTX-NASDAQ) is a global biotechnology company specializing in small molecule drugs for the treatment of serious diseases. Vertex was founded in 1989 and is headquartered in Cambridge, Massachusetts. The Company is developing an oral HCV protease inhibitor, VX-950, for the treatment of hepatitis C. VX-950 is currently in Phase II clinical trials, which is expected to evaluate sustained viral response rates. VX-950 is globally developed by Mitsubishi Pharma Corp., Johnson & Johnson, and Janssen Pharmaceutica, in addition to Vertex.

**ProMetic Life Sciences, Inc.**

ProMetic Life Sciences, Inc. (PLI.SV-TO) is a biopharmaceutical company founded in 1994 and focused on delivering therapeutics that target unmet medical needs worldwide. In ProMetic’s pipeline is PBI-1402, a drug with many applications, most of which are anemia-related. PBI-1402 is a synthetic, orally active drug that ProMetic believes represents a lower cost alternative to EPO treatment for anemia. PBI-1402 is in Phase Ib/II clinical trials.

**Roche Holdings**

Roche Holdings and its products currently on the market are described on page 32. In addition to those products (Roferon-A®, Pegasys®, and Pegasys with Copegus®), Roche has a drug, Continuous Erythropoietin Receptor Activator (CERA), in the development stage. CERA is intended to combat anemia in dialysis patients. It has completed Phase III maintenance studies and recent results have shown that it can raise hemoglobin levels in patients and be administered once every four weeks.

**Schering Plough Corp.**

Schering Plough Corp. and its products currently on the market are described on page 32. In addition, the company is developing oral hepatitis C protease inhibitor capsules that were recently granted Fast Track status by the FDA. These capsules are now in the Phase II clinical trial stage.

**Ambrx, Inc.**

Ambrx, Inc. is a biopharmaceutical company based in La Jolla, California. The company is working to transform protein therapeutics by developing ReCODE™ (reconstituting chemically orthogonal directed engineering) technology. ReCODE™ uses Ambrx’s protein medicinal chemistry to expand current pegylated techniques. Ambrx is combining medicinal chemistry with recombinant biosynthesis to introduce a novel amino acid to a specific site within a protein. ReCODE™ strives to increase the longevity of protein therapy, while maintaining potency. The company’s primary product is a PEG-hGH, ARX-201, which is scheduled to initiate Phase I clinical trials in 2007. Within the company’s pipeline is Ambrx Interferon, which is due to enter the IND stage in late 2007, as well as proteins such as cytokines, peptides, and antibodies, and therapies for cancer, endocrine disorders, inflammation, and infectious disease.
Potential Milestones

Medgenics seeks to accomplish the following events within the next 12-24 months.

**Biopump Technology**

- Present data at a major congress showing achievement of sustained preclinical protein production targets for EPO (EPODURE)
- Present data at a major congress showing achievement of sustained preclinical protein production targets for IFN-α (INFRADURE)
- Complete and validate prototype devices for multi-center use
- Achieve preclinical protein production targets for next protein

**Anemia Product: EPODURE**

- Commence key vector cGMP production
- Obtain regulatory approval for Phase I/II trial in anemia patients
- Enroll first patient for Phase I/II trial in anemia
- Demonstrate therapeutic treatment for four months on first 10 patients
- Enter negotiations for EPO/anemia strategic partnering agreement
- Complete Phase I/II anemia trial

**Hepatitis C Product: INFRADURE**

- Enroll first patient for Phase I/II trial in hepatitis C
- Demonstrate therapeutic treatment for four months on first 10 patients
- Enter negotiations for IFN-α/hepatitis C strategic partnering agreement

**Corporate**

- Medgenics seeks to raise funding to enable the Company to reach readiness to commence Phase I/II efficacy trials of EPODURE to treat anemia in the fourth quarter 2007 and of INFRADURE for hepatitis C, scheduled to commence in the first quarter 2008. As a point of reference, Table 12 (page 36) provides a list of some comparable biomedical transactions that have taken place recently.
<table>
<thead>
<tr>
<th>DATE</th>
<th>COMPANY</th>
<th>RAISED (IN MILLIONS)</th>
<th>PRE-TRANSACTION (IN MILLIONS)</th>
<th>PRODUCT</th>
<th>STATUS AT TIME OF FUNDING</th>
</tr>
</thead>
<tbody>
<tr>
<td>08/2006</td>
<td>Protalix Israel</td>
<td>$15.0</td>
<td>$100.0</td>
<td>therapeutic protein production using plants</td>
<td>Preclinical</td>
</tr>
<tr>
<td>11/2005</td>
<td>GammaCan International Inc.</td>
<td>0.5</td>
<td>37.5</td>
<td>anti-cancer</td>
<td>Phase II</td>
</tr>
<tr>
<td>09/2005</td>
<td>Protalix Israel</td>
<td>5.3</td>
<td>75.0</td>
<td>therapeutic protein production using plants</td>
<td>Preclinical</td>
</tr>
<tr>
<td>08/2005</td>
<td>BrainsGate Ltd.</td>
<td>7.0</td>
<td>28.0</td>
<td>drug delivery device for blood-brain barrier</td>
<td>Preclinical</td>
</tr>
<tr>
<td>08/2005</td>
<td>AngioScore Inc.</td>
<td>2.0</td>
<td>38.0</td>
<td>tools for endovascular therapy scoring balloon catheter</td>
<td>Phase II</td>
</tr>
<tr>
<td>06/2005</td>
<td>Modus Biological Membranes Ltd.</td>
<td>2.5</td>
<td>15.0</td>
<td>pharma to alleviate drug</td>
<td>Preclinical</td>
</tr>
<tr>
<td>05/2005</td>
<td>MetaCure Ltd.</td>
<td>20.0</td>
<td>100.0</td>
<td>electrical therapies for obesity and diabetes</td>
<td>Phase II</td>
</tr>
<tr>
<td>03/2005</td>
<td>Rosetta Genomics Ltd.</td>
<td>4.0</td>
<td>25.0</td>
<td>micro-RNA-based therapeutic drugs</td>
<td>Preclinical</td>
</tr>
<tr>
<td>01/2005</td>
<td>Predix Pharmaceuticals U.S./Israel</td>
<td>43.0</td>
<td>50+</td>
<td>small molecule drugs for Alzheimer’s, depression, and anxiety</td>
<td>Post-Phase I</td>
</tr>
<tr>
<td>08/2003</td>
<td>TransPharma Medical Israel</td>
<td>10.0</td>
<td>15.0</td>
<td>transdermal drug delivery</td>
<td>Preclinical</td>
</tr>
</tbody>
</table>

Source: Medgenics Inc.
Key Points to Consider

- **The Biopump Platform Technology.** Medgenics' Biopump platform technology converts a sliver of the patient’s own dermal tissue into an internal protein production plant, through *ex vivo* transduction with a viral vector and re-implantation of the tissue under the patient's skin. The technology is being developed to produce and deliver natural therapeutic proteins on a sustained basis versus the current standard of frequent, repeat injections of proteins mass produced in animal cells (predominantly rodent cells).

- **Key Product Focus.** Medgenics is currently focusing its Biopump platform technology toward developing two products: EPODURE providing erythropoietin (EPO) to treat anemia, and INFRADURE providing interferon-alpha (IFN-α) to treat hepatitis C.

- **Results Published in Key Journals.** The Company’s Phase I clinical trial (short-action Biopump) and its preclinical research results *in vitro* and in SCID mice have been published in *Blood*, *The Journal of the American Society of Hematology* and in *Molecular Therapy*, a journal by the American Society of Gene Therapy, respectively.

- **Proven Principle in Patients with Short-Action Biopumps.** Proof-of-principle for the Biopump technology (short-action version) and the devices used to implement the procedure was demonstrated in the 2003 Phase I human clinical trial, showing safe, reproducible, and dose-controlled delivery of active EPO in anemic patients, causing the desired formation of new blood cells.

- **Sustained-Action Biopumps.** Medgenics now has a new generation of Biopumps that have reproducibly shown months of sustained production of active EPO and IFN-α in laboratory and mice testing: therapeutic levels continue after more than 160 days *in vitro*. These use a new vector with non-immunogenic properties (“gutless” adeno vector) developed at Baylor College of Medicine (Houston, Texas), where published studies have shown it to provide one to two years of steady high-level protein amounts in normal baboons and in dogs. The Company is preparing to take this sustained-action Biopump to its first efficacy trial in the fourth quarter 2007.

- **Market Opportunities.** Medgenics' Biopump technology addresses the majority of the $51 billion market (as of 2005) for protein therapeutics, aiming to replace more than $30 billion in protein injections each year. In addition, the Company’s platform technology can be easily applied to a range of therapeutic proteins, potentially opening new market segments.

- **Seeking Strategic Partners.** Based on prior discussions with interested companies, Medgenics believes that its sustained-action Biopump technology is likely to be attractive to strategic partners in the pharmaceutical, biotechnology, medical device, and healthcare services sectors. The Company aims to complete its first strategic partnership agreement in the next 18-24 months.

- **Intellectual Property.** The Company’s technology is protected by 48 patents and patent applications in the U.S. and worldwide. This includes one issued U.S. patent, nine pending U.S. patent applications, one issued foreign patent, and 37 pending foreign patent applications.

- **Management.** Medgenics is managed by a team of individuals with decades of experience in biotechnology and biomedical devices, together with professionals from the healthcare, finance, medical, and academic communities. The Company's Board of Directors includes current and former directors of international healthcare companies, and its Scientific Advisory Board (SAB) includes past presidents of the American Society of Renal Physicians, the American Gastroenterological Association, and the American Society of Gene Therapy.

  - Dr. Andrew Pearlman, the Company's current chief executive officer, raised $17 million of the Company's funding in four equity rounds and took the Company through its first clinical trial. Medgenics is currently working to raise funds intended to drive completion of preclinical preparations and readiness for the commencement of Phase I/II efficacy trials for its two main products, EPODURE and INFRADURE, by the fourth quarter 2007 and the first quarter 2008, respectively.
Historical Financial Results

Tables 13, 14, and 15 provide a summary of Medgenics’ key historical financial statements through 2004—its Statements of Operations, Balance Sheets, and Statements of Cash Flows, noting that in late 2003, following escalating conflicts among different individuals within management regarding the direction of the Company, an unsuccessful change in management led to subsequent cessation of operations in the third quarter 2004. In a clean restart of the Company, Dr. Pearlman raised initial relaunch funding of $1.1 million from private investors in a completely reorganized and recapitalized structure, converting all outstanding loans and previous shares (Common and Preferred) into a single class of Common Shares as of March 31, 2006. Since this restart, the Company’s initial core team has resumed active development work, and by October 2006, had developed new sustained-action Biopumps for anemia (EPODURE) and hepatitis C (INFRADURE), demonstrating over five months of sustained therapeutic protein levels in vitro and in animals. It is to be noted that since the financial results below only cover the period through 2004, which preceded this restart and reorganization, they do not reflect the current capital or financial status, and thus should be viewed in this context.

<table>
<thead>
<tr>
<th>Table 13</th>
<th>Medgenics Inc.</th>
</tr>
</thead>
<tbody>
<tr>
<td>CONSOLIDATED STATEMENTS OF OPERATIONS (in U.S. Dollars)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Year ended December 31, 2004</td>
</tr>
<tr>
<td>Research and development expenses, net</td>
<td>2,471,879</td>
</tr>
<tr>
<td>General and administrative expenses</td>
<td>1,535,913</td>
</tr>
<tr>
<td>Operating loss</td>
<td>4,007,792</td>
</tr>
<tr>
<td>Financial expenses, net</td>
<td>89,266</td>
</tr>
<tr>
<td>Other expenses</td>
<td></td>
</tr>
<tr>
<td>Loss from sales of property and equipment</td>
<td>319,930</td>
</tr>
<tr>
<td>Loss before taxes on income</td>
<td>4,416,988</td>
</tr>
<tr>
<td>Taxes on income</td>
<td>2,825</td>
</tr>
<tr>
<td>Net loss</td>
<td>4,419,813</td>
</tr>
</tbody>
</table>

Source: Medgenics Inc.
Table 14
Medgenics Inc.
CONSOLIDATED BALANCE SHEETS (in U.S. Dollars except for share amounts)

<table>
<thead>
<tr>
<th>December 31,</th>
<th>2004</th>
<th>2003</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2004</td>
<td>2003</td>
</tr>
<tr>
<td><strong>ASSETS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CURRENT ASSETS:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cash and cash equivalents</td>
<td>181,692</td>
<td>1,889,151</td>
</tr>
<tr>
<td>Accounts receivable and prepaid expenses</td>
<td>336,860</td>
<td>662,246</td>
</tr>
<tr>
<td>Total current assets</td>
<td>518,552</td>
<td>2,551,397</td>
</tr>
<tr>
<td>SEVERANCE PAY FUND</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PROPERTY AND EQUIPMENT, NET</td>
<td>19,034</td>
<td>577,654</td>
</tr>
<tr>
<td>Total assets</td>
<td>570,891</td>
<td>3,397,272</td>
</tr>
<tr>
<td><strong>LIABILITIES AND SHAREHOLDERS' EQUITY</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CURRENT LIABILITIES:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short-term bank credit and current maturities of long-term loans</td>
<td>—</td>
<td>90,298</td>
</tr>
<tr>
<td>Trade payables</td>
<td>8,756</td>
<td>202,397</td>
</tr>
<tr>
<td>Other accounts payable and accrued expenses</td>
<td>1,690,394</td>
<td>468,156</td>
</tr>
<tr>
<td>Total current liabilities</td>
<td>1,699,150</td>
<td>760,851</td>
</tr>
<tr>
<td>LONG-TERM LIABILITIES:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Long-term loans, net of current maturities</td>
<td>—</td>
<td>1,455</td>
</tr>
<tr>
<td>Accrued severance pay</td>
<td>33,305</td>
<td>274,407</td>
</tr>
<tr>
<td>Total long-term liabilities</td>
<td>33,305</td>
<td>274,407</td>
</tr>
<tr>
<td><strong>COMMITMENTS AND CONTINGENCIES</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SHAREHOLDERS’ EQUITY (DEFICIENCY):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Common shares - $0.0001 Par Value, 17,000,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shares Authorized at December 31, 2004 and 2003, 3,514,089 and 3,468,006 Shares Issued and Outstanding at December 31, 2004 and 2003, respectively.</td>
<td>351</td>
<td>347</td>
</tr>
<tr>
<td>Preferred shares - Series A - $0.0001 Par Value, 8,448,678</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shares Authorized at December 31, 2004 and 2003, 4,224,339</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shares Issued and Outstanding at December 31, 2004 and 2003. Aggregate Liquidation Preference of Approximately $9,631,259 and $8,917,832 at December 31, 2004 and 2003, respectively.</td>
<td>422</td>
<td>422</td>
</tr>
<tr>
<td>Preferred shares - Series B - $0.0001 Par Value, 15,000,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shares Authorized at December 31, 2004 and 2003, 3,743,671</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shares Issued and Outstanding at December 31, 2004 and 2003. Aggregate Liquidation Preference of Approximately $6,369,028 and $5,897,248 at December 31, 2004 and 2003, respectively.</td>
<td>375</td>
<td>375</td>
</tr>
<tr>
<td>Additional Paid-in Capital</td>
<td>17,269,681</td>
<td>16,912,796</td>
</tr>
<tr>
<td>Deferred Stock Compensation</td>
<td>—</td>
<td>(539,801)</td>
</tr>
<tr>
<td>Deficit Accumulated During the Development Stage</td>
<td>(18,432,393)</td>
<td>(14,012,580)</td>
</tr>
<tr>
<td>Total shareholders’ equity (deficiency)</td>
<td>(1,161,564)</td>
<td>2,361,559</td>
</tr>
<tr>
<td>Total liabilities and shareholders’ equity</td>
<td>570,891</td>
<td>3,397,272</td>
</tr>
</tbody>
</table>

*Source: Medgenics Inc.*
Table 15  Medgenics Inc.  
CONSOLIDATED STATEMENTS OF CASH FLOWS (in U.S. Dollars)  

<table>
<thead>
<tr>
<th>Year ended December 31</th>
<th>Period from inception</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2004</td>
</tr>
<tr>
<td><strong>CASH FLOWS FROM OPERATING ACTIVITIES:</strong></td>
<td></td>
</tr>
<tr>
<td>Net loss</td>
<td>(4,419,813)</td>
</tr>
<tr>
<td>Adjustments to reconcile net loss to net cash used in operating activities:</td>
<td></td>
</tr>
<tr>
<td>Depreciation</td>
<td>104,723</td>
</tr>
<tr>
<td>Erosion of long-term loans</td>
<td>1,544</td>
</tr>
<tr>
<td>Loss from sales of property and equipment</td>
<td>319,930</td>
</tr>
<tr>
<td>Interest on convertible loan</td>
<td>92,858</td>
</tr>
<tr>
<td>Amortization of deferred stock compensation</td>
<td>539,801</td>
</tr>
<tr>
<td>Stock-based compensation related to options and shares to consultants</td>
<td>356,762</td>
</tr>
<tr>
<td>Accrued severance pay, net</td>
<td>(5,186)</td>
</tr>
<tr>
<td>Increase (decrease) in trade payables</td>
<td>(193,641)</td>
</tr>
<tr>
<td>Decrease (increase) in other accounts receivable and pre-paid expenses</td>
<td>325,386</td>
</tr>
<tr>
<td>Increase (decrease) in other accounts payable and accrued expenses</td>
<td>(417,845)</td>
</tr>
<tr>
<td>Net cash used in operating activities</td>
<td>(3,295,481)</td>
</tr>
<tr>
<td><strong>CASH FLOWS FROM INVESTING ACTIVITIES:</strong></td>
<td></td>
</tr>
<tr>
<td>Proceeds from sales of property and equipment</td>
<td>158,081</td>
</tr>
<tr>
<td>Purchase of property and equipment</td>
<td>(24,114)</td>
</tr>
<tr>
<td>Net cash provided by (used in) investing activities</td>
<td>133,967</td>
</tr>
<tr>
<td><strong>CASH FLOWS FROM FINANCING ACTIVITIES:</strong></td>
<td></td>
</tr>
<tr>
<td>Proceeds from issuance of shares, net</td>
<td>127</td>
</tr>
<tr>
<td>Proceeds from long-term loans</td>
<td>—</td>
</tr>
<tr>
<td>Repayment of long-term loans</td>
<td>(23,595)</td>
</tr>
<tr>
<td>Proceeds from convertible loan</td>
<td>1,547,225</td>
</tr>
<tr>
<td>Increase (decrease) in short-term bank credit</td>
<td>(69,702)</td>
</tr>
<tr>
<td>Net cash provided by financing activities</td>
<td>1,454,055</td>
</tr>
<tr>
<td>Increase (decrease) in cash and cash equivalents</td>
<td>(1,707,459)</td>
</tr>
<tr>
<td>Balance of cash and cash equivalents at beginning of the period</td>
<td>1,889,151</td>
</tr>
<tr>
<td>Balance of cash and cash equivalents at end of the period</td>
<td>181,692</td>
</tr>
</tbody>
</table>

**Supplemental disclosure of cash flows information:**
Cash paid during the period for:

| Interest | 567 | 5,828 | 22,288 |
| Taxes    | 2,825 | 48,912 | 53,251 |

*Source: Medgenics Inc.*
Risks

Some information in this report relates to future events or future business and financial performance. Such statements can be only predictions and the actual events or results may differ from those discussed. The content of this report with respect to Medgenics has been compiled primarily from information available to the public and released by Medgenics through news releases and various publications. Medgenics is solely responsible for the accuracy of that information. Information about other companies has been prepared from publicly available documents and has not been independently verified by Medgenics. For more information about Medgenics, please refer to the Company’s website at www.medgenics.com.

One should carefully consider the risks and the information about Medgenics’ business described below. One should not interpret the order in which these considerations are presented as an indication of their relative importance. The risks and uncertainties described below are not the only ones the Company faces. Additional risks and uncertainties not presently known or those it currently considers immaterial may also have an adverse effect on its business. If any of the matters discussed in the accompanying risk factors were to occur, Medgenics’ business, financial condition, results of operations, cash flows, or prospects could be materially adversely affected. For some of the risks listed, the Company suggests its intended solution to respond to or reduce the risk.

COMPANY SPECIFIC

There is no public market for the Company’s stock.

There is no public market for Medgenics’ securities. As a result, the purchasers of the Common Shares may not be able to liquidate their investment readily, if at all.

Solution. The Company plans to transition to public status in the near future.

Medgenics has significant international operations, including in Israel, which may be adversely affected by acts of terrorism, major hostilities, adverse legislation, or litigation.

Medgenics is a U.S.-based company with a wholly owned subsidiary in Karmiel, Israel. Therefore, any acts of terrorism, hostilities, adverse legislation, or litigation in either of these countries may affect Medgenics’ operations. The Company’s operations could be materially and adversely affected by acts of terrorism. If major hostilities should occur in the Middle East, including as a result of acts of terrorism in the U.S. or elsewhere, any such effects may not be covered by insurance.

Solution. As in the recent Lebanese/Israeli conflict, Medgenics took the appropriate steps to assure the Company’s operations continued. Throughout the conflict during the summer of 2006, Medgenics successfully, efficiently, and temporarily relocated key operations to the south. Company activity continued as usual with both science and business activities progressing positively. Prior to this, Medgenics’ key management has had decades of experience in life science technology business in Israel maintaining uninterrupted business activity despite political events or hostilities in the region.

The Company is subject to extensive government regulation in several countries.

Medgenics is subject to regulatory requirements in all countries where it operates and desires to introduce its product. These requirements range from vector and Biopump potency to long-term follow-up on treated patients. The clearance and approval process from both the U.S. Food and Drug Administration (FDA) and foreign regulatory authorities can be costly, time consuming, and uncertain.

Solution. Medgenics is closely guided by top regulatory advisors who were former FDA officers, including Dr. Michael Hensley and Dr. Andra Miller (biographies on page 12 and 13, respectively). Dr. Miller, formerly with the FDA’s Center for Biologics Evaluation and Research (CBER)’s Cellular and Gene Therapies Division, is now a leading consultant in this area. With their guidance and assistance, the Company has succeeded thus far in maintaining positive cooperation with the FDA through the
successful Phase I proof-of-principle trial and was recently invited by the FDA’s director of Cell and Gene Therapy, Dr. Stephanie Simek, to a pre-Investigational New Drug (IND) meeting.

The Company hopes to obtain Phase I/II approval from the Israeli Ministry of Health (MOH) in time to start clinical trials in the fourth quarter 2007. Medgenics’ ability to further test its products and technologies in clinical trials is contingent upon this approval. There can be no assurance that the Company will receive these clearances or that it will have sufficient resources to complete the regulatory approval process.

**Solution.** Medgenics has received approval from the Israeli MOH for its almost identical clinical protocol in 2003, and the same principal investigator believes approval in the proposed timeframe is a reasonable expectation for the new study. Therefore, the risk is reduced with respect to receiving approvals in the future.

It typically takes a company several years or longer to satisfy the substantial requirements imposed by the FDA and comparable agencies in other countries for the introduction of therapeutic pharmaceutical and biological products. Delays in obtaining such clearances could have a material adverse effect on the Company, while changes in existing requirements could also have a material adverse effect on the Company. Failure to obtain required regulatory approvals could require the Company to curtail or cease its operations. Even if Medgenics invests the necessary time, money, and resources required to advance through the FDA approval process, there is no guarantee that the Company will receive FDA approval of its products.

**Solution.** The Company is working with the top ex-FDA regulatory advisors in order to properly guide it through the difficult regulatory approval process.

Medgenics is also subject to regulation in Israel. Pharmaceutical products must be registered in accordance with applicable law before they can be manufactured, marketed, etc. This registration must include medical data proving the product’s safety, efficacy, and clinical testing. Also included in product registration should be references to medical publications and information about the production methods and quality control. Health ministries may cancel a product’s registration if it is found harmful, ineffective, or improperly manufactured or marketed.

**Solution.** In addition to the substantial guidance from FDA regulatory and clinical development experts, Medgenics is guided in Israel by its principle investigators who have extensive experience in clinical development and regulatory processes in Israel. Furthermore, the Company works closely with the ethical (Helsinki) committees and the Israeli MOH in planning the study protocols and their implementation, as well as works with local branches of internationally respected Contract Research Organizations (CROs) in the management of the clinical trials.

**The Company’s intellectual property contains a significant number of pending patents.**

The Company’s patent portfolio contains two issued patents and 46 U.S. and foreign pending patents. There is no guarantee that the Company will obtain patents in the other countries in which patent applications have been or will be filed, or that it will develop other patentable products or processes. In addition, there can be no assurance that any future patents will prevent other companies from developing similar or medically equivalent products, or that other companies will not be issued patents that may prevent the sale of Company’s products or that will require licensing and the payment of significant fees or royalties by the Company. Furthermore, issued patents may not be valid or enforceable, or be able to provide meaningful protection to the Company. Patent litigation is costly and time-consuming, and there can be no assurance that the Company will have or will devote sufficient resources to pursue such litigation.

**Solution.** The Company’s patent counsel believes that the key patent claims will be issued and will provide protection.

The Company’s ability to commercialize the Biopump technology as well as its other products will depend, in part, on its ability both in the U.S. and in other countries to obtain patents, enforce those patents, preserve trade secrets, and operate without infringing on proprietary rights of third parties. To minimize its risk of infringing on currently available technology, Medgenics has conducted a Freedom to
Operate (FTO) analysis. As a result of such, the Company’s position is that it does not infringe on the Amgen portfolio since the Company uses only the nucleic acid sequence, which is now public domain. After implantation of the Biopump, the patient’s natural mechanism produces the EPO. There is no assurance that the FTO attains absolute certainty of non-infringement.

Solution. While there is no absolute assurance, the Company notes that the chief patent counsel of a potential strategic partner company with which Medgenics has been in contact, has reviewed the FTO and concurred with Medgenics’ patent counsel.

It may take the Company longer to obtain third-party reimbursement for its products than expected, despite cost-saving advantages to third-party payers, and changing healthcare industries could affect the commercialization of the Company’s product.

In the U.S., suppliers of healthcare products and services are greatly affected by Medicare, Medicaid, and other government insurance programs, as well as by private insurance reimbursement programs. Pharmaceutical pricing is also subject to regulation in Israel as well as other countries within which the Company may wish to provide its product. Healthcare reform is often a subject of attention in governments that are trying to contain healthcare expenditures. Healthcare reform proposals are common in the U.S. Congress and some state legislatures, as well as in other countries. There is no assurance that legislation resulting in adverse effects for the Company will not be adopted in a country in which the Company operates.

In addition, third-party payers (Medicare, Medicaid, private health insurance companies, and other organizations) may affect the pricing or relative attractiveness of the Company’s product by regulating the level of reimbursement provided to the physicians and clinics utilizing the Biopump technology or by refusing reimbursement. If the Biopump technology is not reimbursed under these programs or if the amount of time to acquire reimbursement is too long, the Company’s ability to market its product may be materially and/or adversely affected, even though the Company expects to be able to provide cost-saving advantages that would make the product attractive to third-party payers. In international markets, reimbursement by private third-party medical insurance providers, including government insurers and independent providers, varies from country to country. In certain countries, Medgenics’ ability to achieve significant market penetration may depend upon the availability of third-party government reimbursement.

Solution. Medgenics is assisted in this by several of its key advisors and directors, some of whom have extensive experience in negotiating reimbursement policy with the Centers for Medicare and Medicaid Services (CMS) and third-party payers. In addition, the Company intends to retain top advisors on specific reimbursement strategies for configurations of Biopump therapy implementation.

Medgenics is a development stage company, and as such, has not generated any revenue to date.

The Company has not generated significant profits to date from its proposed business or operations. Moreover, the Company may not be able to generate either revenue or profit in the foreseeable future.

In order to continue the development of the Biopump technology, the Company has a significant future capital need.

The Company currently has no significant operations from which to generate cash flow. The Company’s future capital requirements will depend on many factors, including current and planned fundraising efforts and the Company’s ability to acquire strategic partners for its Biopump technology and related protein pipeline. Medgenics hopes to raise funding in the first quarter 2007. These funds are intended to drive completion of preclinical preparations and readiness for the commencement of the EPODURE and INFRADURE efficacy trials, as well as to bring the device prototypes up to preproduction performance (enabling multi-center clinical trials).

Alternatives for raising these funds may include a public offering or mezzanine funding leading to a public offering. If adequate funds are not obtained, the Company may be required to reduce or curtail its proposed operations.
The Company could encounter difficulty with the development of its technology or devices.

Medgenics is working to perfect devices used in the implementation of its Biopump technology. The Company expects that these devices will be capable of cost-effective, reliable execution of the Biopump procedure at widely dispersed treatment centers on a range of patients. However, unforeseen funding or technical difficulties may cause the development of these devices to take longer and cost more than planned. In addition, only new clinical trials can prove the duration of the sustained-action Biopumps. A potential problem that may arise in this trial is an unexpected immune reaction to the viral vector in the patients.

Solution. Based on the advice of many experts, the Company views immune reaction as unlikely, but should it occur, believes it is possible to switch to another viral vector (such as the adeno-associated virus [AAV] double stranded) or a non-viral vector instead. Medgenics’ management has extensive experience in device development and production and is preparing alternate development strategies through R&D in order to anticipate hurdles in technology development. The Company’s efforts toward development of alternative vectors and non-viral vectors is an example of this type of alternate development strategy.

SECTOR SPECIFIC

There is significant competition in the biopharmaceutical industry, including in the field of protein therapeutics.

The biopharmaceutical industry is highly competitive. Medgenics competes with other companies that develop products to treat the same diseases. Many of these companies have considerably greater resources than the Company, and while Medgenics does present a unique protein delivery technology, there is no guarantee that the products developed by other companies will not cause the Company’s products and technologies to become less competitive or even obsolete. Table 10 (page 31) and Table 11 (page 33) summarize Medgenics’ competitors/potential competitors.

Solution. The Company believes its technology offers advantages over existing technologies, and it continues to improve and enhance its technology through ongoing R&D and new application development.
Publications


08/02/2005—Published in *Molecular Therapy*, a journal by the American Society of Gene Therapy, an article titled “*Ex Vivo* Transduction of Human Dermal Tissue Structures and **Autologous** Implantation Production and Delivery of Therapeutic Proteins.” The article discusses Medgenics’ Biopump technology and *ex vivo* transduction at length.
Glossary

**Acquired Immune Deficiency Syndrome (AIDS)**—The late stage of Human Immunodeficiency Virus (HIV) disease, characterized by a deterioration of the immune system and a susceptibility to a range of opportunistic infections and cancers.

**Acute**—Having a short and relatively severe course.

**Adeno vector**—A genetically modified, non-replicating adenovirus capable of efficiently carrying therapeutic genes into cells. Adeno vectors produce high titers, efficiently infect a broad range of cell types, and infect dividing and non-dividing cells. These vectors are also widely reported to have toxic and immunogenic effects owed to the production of immunogenic viral proteins.

**Adeno virus**—Any of a group of deoxyribonucleic acid (DNA)-containing viruses that cause conjunctivitis and upper respiratory tract infections in humans.

**Amino acid**—Any of a class of organic compounds that contains at least one amino group, –NH₂, and one carboxyl group, –COOH. The alpha-amino acids, RCH(NH₂)COOH, are the building blocks from which proteins are constructed.

**Anemia**—A shortage of red blood cells that causes symptoms of fatigue, weakness, pallor, and shortness of breath. Approximately two-thirds of cancer patients undergoing chemotherapy become anemic since chemotherapy or radiotherapy treatments often result in a decrease of erythrocytes in the general circulation. Anemia is also associated with end-stage renal disease (ESRD), as is the situation for patients who require regular dialysis or kidney transplants for survival.

**Aplastic anemia**—A rare and serious condition in which the bone marrow stops producing enough red and white blood cells to keep the body healthy, resulting in an increased risk of infection and uncontrollable bleeding.

**Arrhythmia**—An irregular heartbeat. In an arrhythmia, the heart either beats too fast or too slow.

**Autologous**—Derived or transferred from the same individual’s body: autologous blood donation; an autologous bone marrow transplant.

**Bolus injections**—The injection of a drug (or drugs) in a high quantity (called a bolus) at once.

**Bone marrow**—The soft, sponge-like tissue in the center of bones that produces white blood cells, red blood cells, and platelets.

**Chronic kidney disease (CKD)**—A condition which occurs when the kidneys cannot do their job of cleaning blood of toxins and waste products. Anemia is a common complication of chronic kidney disease (CKD) because the kidneys are unable to manufacture enough erythropoietin, a hormone that regulates the production of red blood cells. Diabetes and high blood pressure are two main causes of CKD.

**Cirrhosis**—A liver condition often associated with chronic hepatitis, alcoholism, or non-alcoholic fatty liver disease. This condition, in which healthy liver tissue is replaced by fibrous tissue and followed by a scar-like hardening, can lead to liver failure. Symptoms associated with cirrhosis include fluid retention (which causes swelling in the stomach, legs, or entire body), persistent jaundice, fatigue, disturbances in sleeping, itchy skin, loss of appetite, weight loss, vomiting blood, and mental disturbances.

**Cohort**—Groups of individuals who share one or more characteristics in a research study and who are followed over time. For example, a vaccine trial might include two cohorts: a group at low risk for HIV and a group at a higher risk.

**Congestive heart failure (CHF)**—Any condition in which the heart is unable to adequately perform its function of pumping blood throughout the body and/or prevent blood from backing up into the lungs. CHF is not a specific disease, but rather a symptom of impairment caused by an underlying disease.
Crohn's disease — A chronic inflammatory condition primarily involving the small and large intestine. Mild forms of the disease can cause small ulcers on the inner surface of the bowel, while severe forms yield deeper and larger ulcers that can lead to infection in the abdominal cavity and surrounding organs.

Current Good Manufacturing Practices (cGMP) — A standard used by pharmaceutical, medical device, and food manufacturers as they produce and test products that people use. Drug cGMPs also apply to veterinary drugs.

End-stage renal disease (ESRD) — Severe kidney disease or chronic kidney failure that has reduced the kidney function to 10% or less of normal function, requiring the patient to have either dialysis or a transplant in order to live. Also called renal failure.

Erythrocytes — A cell in the blood of vertebrates that transports oxygen and carbon dioxide to and from the body's tissue. In mammals, the red blood cell is disk-shaped and biconcave, contains hemoglobin, and lacks a nucleus. Also called red blood cells.

Erythropoiesis — The process of producing red blood cells by stimulating the stem cells in the bone marrow.

Erythropoietin (EPO) — A glycoprotein hormone that stimulates the production of red blood cells by stem cells in bone marrow. Produced mainly by the kidneys, it is released in response to decreased levels of oxygen in body tissue.

Ex vivo — In an artificial environment outside the living organism.

Factor VIII — The clotting factor protein absent or decreased in patients with Hemophilia A. Also called anti-hemophilic factor.

Fast Track — A formal mechanism to interact with the FDA using approaches that are available to all applicants for marketing claims.

Folate — A B-complex vitamin that is being studied as a cancer prevention agent. Also called folic acid.

Freedom to Operate — The advice rendered by a patent attorney with respect to whether a technology will infringe a third party's patent. A FTO typically involves a 'product clearance' investigation to proactively identify and dispose of patents in the area of the entity’s products, thereby proactively reducing the risk of subsequent patent problems.

Glycosylation — The addition of glycosyl groups to a protein to form a glycoprotein.

Granulocyte-colony stimulating factor (G-CSF) — A glycoprotein, growth factor, or cytokine produced by a number of different tissues to stimulate the bone marrow to produce granulocytes. It also stimulates the survival, proliferation, differentiation, and function of neutrophil granulocyte progenitor cells and mature neutrophils.

Half-life — Time needed for the plasma concentration or the amount of drug in the body to be reduced by 50%.

Harvest — To remove from a culture or a living or dead body, as for the purposes of transplantation.

Helper-Dependent Adeno vector (HDAd) — Also known as "gutless Adeno", HD Adeno vectors have had all their viral coding sequences deleted, and therefore have no viral genes and thus cannot express any viral proteins. For these reasons, HD Adeno vectors are believed to be non-immunogenic.

Hematocrit — A test measuring the percent of red cells in a sample of whole blood; used to test for anemia.

Hemoglobin — A protein produced within the bones that enables red blood cells to transport oxygen throughout the body. Hemoglobin, when in contact with oxygen, also gives red blood cells their color.

Hemolytic anemia — Red blood cells have a normal life span of approximately 90-120 days, at which time the old cells are destroyed and replaced by the body’s natural processes. Hemolytic anemia is a disorder
in which the red blood cells are destroyed prematurely. The cells are broken down at a faster rate than
the bone marrow can produce new cells. Hemoglobin, the component of red blood cells that carries
oxygen, is released when these cells are destroyed.

Hepatitis C—Previously known as non-A, non-B hepatitis, hepatitis C is an inflammation of the liver,
which causes fever, jaundice, abdominal pain, and weakness. Unlike other forms of hepatitis, hepatitis C
is largely caused by blood transfusions, contaminated needles, and in rare cases, sexual contact.

Hepatitis C virus (HCV)—A non-A, non-B RNA virus causing post-transfusion hepatitis and commonly
found in individuals who have used illegal injection drugs.

Human EPO (hEPO)—A hormone produced by the kidney that promotes the formation of red blood cells
in the bone marrow. EPO is a glycoprotein (a protein with a sugar attached to it).

Human growth hormone (hGH)—A hormone produced in the pituitary gland that assists in the
stimulation of another hormone called somatomedin in the liver, which causes growth.

Immunogenicity—The property of being able to evoke an immune response within an organism.
Immunogenicity depends partly upon the size of the substance in question and partly upon how unlike
host molecules it is. Highly conserved proteins tend to have rather low immunogenicity.

In vitro—In the laboratory (outside the body). The opposite of in vivo (in the body).

In vivo—In the body (opposite of in vitro).

Interferon-alpha (IFN-α)—An interferon produced by white blood cells that inhibits viral replication,
suppresses cell proliferation, and regulates immune response. It is currently used in a form obtained from
recombinant DNA to treat various diseases.

Interferon-beta (IFN-β)—An interferon produced especially by fibroblasts that is used in a form obtained
from recombinant DNA, especially in the treatment of MS marked by recurrent attacks alternating with
periods of remission.

Kaposi’s sarcoma—Type of cancer characterized by abnormal growths of blood vessels that develop into
purplish or brown lesions.

Micro-organ (MO)—A proprietary tissue structure made from an excised sliver of tissue taken directly
from a patient or animal, which can be maintained as functioning tissue for extended periods of time in
laboratory conditions. This unusual capability is made possible by the fact that the MO has a sufficient
number of cell layers to compose a functional tissue. It has various cell types in a cellular architecture as
found in the original tissue and has sufficiently small key dimensions that permit its cells to receive
nutrients and remove waste via passive diffusion. MOs can be made from various tissues, (e.g., the lower
portion of the skin). They can be processed into Biopumps, which manufacture and distribute required
therapeutic proteins after implantation back into the patient.

Neocytolysis—Selective destruction of the youngest circulating red blood cells likely caused by a fall in
erythropoietin below a threshold.

Non-immunogenic—Not producing an immune response.

Oncology—The branch of medicine that deals with tumors, including study of their development,
diagnosis, treatment, and prevention.

Passive diffusion—Involves the movement of drug molecules down a concentration or electrochemical
gradient without the expenditure of energy. The rate is directly proportional to the gradient; it is not able to
be saturated, and thus cannot be inhibited by other drugs unless the physical properties of the drug or
membrane are affected in some way.

Pegylated or PEGylation—A process of attaching one or more chains of a substance called
polyethylene glycol (also known as PEG) to a protein molecule such as interferon.
Pernicious anemia—A rare disease state that comes about when the body cannot absorb enough vitamin B-12. The body becomes unable to produce enough red blood cells, resulting in fatigue, a fast pulse, sore mouth and tongue, and weight loss.

Platelet-derived growth factor (PDGF)—A glycolytic protein released by platelets and other cells that stimulates growth of cells of mesenchymal origin, for example, bone cartilage, vascular tissue, and connective tissue.

Polyethylene glycol (PEG)—A polymer made from ethylene oxide which is similar to some non-ionic detergents. Not considered toxic, it takes large doses to be lethal in animals. However, PEG is slow to degrade and is synthetic.

Proof-of-principle—Proof-of-principle research aims to provide evidence for the impact of new, alternative disease control tools and approaches. On the basis of such evidence, current disease control strategies may be improved.

Protease inhibitor—One of a class of anti-HIV drugs designed to inhibit the enzyme protease and interfere with virus replication. Protease inhibitors prevent the cleavage of HIV precursor proteins into active proteins, a process that normally occurs when HIV replicates.

Pure red cell aplasia (PRCA)—A condition in which RBC precursors in bone marrow are nearly absent, while megakaryocytes and white blood cell (WBC) precursors are usually present at normal levels.

Radiofrequency (RF)—An invasive procedure that involves heating tissue in order to destroy it. Used to treat some types of rapid heart rhythms.

Recombinant proteins—Proteins with amino acid sequences encoded by a cloned gene.

Reticulocyte—An immature red blood cell that contains a network of basophilic filaments.

Severe Combined Immunodeficient (SCID) mice—Mice that lack both T and B lymphocytes and are used for transplantation and study of human lymphoid tissues resulting in a SCID-human mouse chimera.

Sickle cell anemia—A chronic, usually fatal anemia marked by sickle-shaped red blood cells, occurring almost exclusively in Blacks from Africa or of African descent, and characterized by episodic pain in the joints, fever, leg ulcers, and jaundice. The disease occurs in individuals who are homozygous for a mutant hemoglobin gene.

Subcutaneous—Occurring below the surface of the skin.

Sustained virologic response (SVR)—Having no virus in the blood six months after finishing treatment.

Thalassemia—A group of genetic blood disorders characterized by a defect in the ability to produce hemoglobin, leading to the rupturing of red blood cells (called hemolytic anemia).

Transduced—See transduction (below).

Transduction—The transfer of bacterial DNA by phages from an infected bacterium to another bacterium. This also refers to the transfer of genes into eukaryotic cells by viruses. This naturally occurring process is routinely employed as a gene transfer technique.

Viral vector—A type of virus used in protein therapy and in cancer therapy.
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