

# QUARTERLY UPDATE

## Business Update on Medgenics Inc.

### Snapshot

February 27, 2009

Medgenics Inc. is a clinical-stage biopharmaceutical company developing a platform technology to provide sustained-action protein therapy for chronic diseases, initially 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 a patient's own skin. Directly addressing a protein therapeutic market forecast to be \$87 billion by 2010, the Biopump works inside the body to produce and deliver active protein steadily for a sustained duration to treat a targeted indication. The platform employs a sliver of dermal tissue, which is harvested from under the patient's skin and engineered to manufacture and distribute the required therapeutic protein using well-established protein production methods. The tissue is processed *ex vivo* using a viral vector having non-immunogenic properties, which carries the appropriate gene into the nuclei of the tissue's cells and causes them to produce the selected protein, converting the dermal tissue into a sustained-action Biopump. In 10 to 14 days after the harvest, the Biopump is reinserted into the patient in order to supply the active protein to the patient for more than three months. A protein production plant in the patient, the Biopump is intended to replace the need for frequent, costly, and painful injections and avoid their side effects. The Company is currently developing its first two products based on its sustained-action Biopump technology: (1) EPODURE producing EPO to treat anemia; and (2) INFRADURE producing interferon-alpha (IFN- $\alpha$ ) to treat hepatitis C. The Biopump platform is also intended to produce other proteins to treat conditions such as multiple sclerosis, hemophilia, pediatric growth deficiencies, and diabetes, among others.



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### Recent Financial Data

Ticker (Exchange)	MEDG (AIM)*
Recent Price (02/26/2009)	£0.0325
52-week Range	£0.0150 - £0.0924
Shares Outstanding	118.4 million
Market Capitalization	£3.85 million
Average 3-month Volume	9,665
Insider Owners	29.4%
Institutional + 5% Owners	60.5%
EPS (6 months ended 06/30/2008)	(\$0.03)
Employees	18



\* Share data (except EPS) is in the British Pound.  
On 02/26/2009, £1.00 = ~US\$1.43.

### Key Points

- In February 2009, Medgenics reported more than four months of sustained anemia treatment in the first two patients in a Phase I/II clinical trial of EPODURE's safety and efficacy, which commenced in August 2008. Data has shown that hemoglobin levels in both participants were sustained in the target range to treat their anemia for at least four months without any EPO injections. Such patients normally would receive up to 50 EPO injections during this same period. To date, six patients have been treated with the low dose of EPODURE, and most have shown sustained hemoglobin levels. In addition, no serious adverse effects have been reported thus far. The next patients are scheduled to be treated with the next highest dose.
- Medgenics believes that its clinical trial is not only demonstrating the safety and efficacy of EPODURE but results are already validating the concept of the Biopump platform as an innovative approach of sustained protein therapy to treat chronic diseases. The Company reports that the ongoing clinical results are also stimulating significant partnering interest from major corporations.
- Medgenics' technology is protected by over 44 patents and patent applications worldwide, which relate to all aspects of the Biopump platform from tissue engineering to its use treating disease. In December 2008, the Company received its most recent U.S. patent, which covers key claims for the Biopump technology in the U.S.
- In May 2008, the Company appointed its vice president of clinical affairs, Dr. Ehud Shoshani, a former medical director and chief executive officer (CEO) of Quintiles Israel. Medgenics continues to receive ongoing government funding from Israel's Office of the Chief Scientist and has recently raised \$430,000 through the exercise of Warrants by existing shareholders. The Company is also in the process of raising further funds to support the ongoing clinical trial, development, and testing of the Biopump platform and associated products.

## Key Recent Events

*Presented in U.S. dollars, unless otherwise noted.*

An overview of the Company's recent news is provided below, referring the reader to Medgenics' website for complete press releases ([www.medgenics.com](http://www.medgenics.com)).

- *On February 3, 2009*, Medgenics announced that the EPODURE Biopump successfully demonstrated safety and efficacy for the sustained protein therapy of anemia in patients with chronic kidney disease (CKD). In the Company's ongoing Phase I/II clinical trial, a one-time administration of EPODURE, producing and delivering the low dose of 18-25 IU/kg/day of the protein erythropoietin (EPO), was sufficient to sustain therapeutic elevation of hemoglobin in most patients. The earliest patients to receive treatment have shown sustained hemoglobin within the target range for four months without receiving any EPO injections. By contrast, in standard practice today, EPO injections may be required up to several times per week, and the comparable low dose is not believed to result in sufficient hemoglobin levels in most patients. The next patients are scheduled to be treated with the next highest dose.
- *On December 23, 2008*, Medgenics announced that it received formal notification from the United States Patent and Trademark Office (USPTO) that a patent would be issued on December 23, 2008, for the key claims covering a core element of the Biopump protein therapy technology. The Company believes that these claims are the most important to the protection of its core dermis Biopump technology. The patent—patent number 7,468,242—represented a significant milestone in protecting key elements of Medgenics' intellectual property in the U.S., the Company's largest target market for the Biopump platform technology. Additional claims from the same application are under review by the USPTO, and applications for patents with similar claims are pending in other key jurisdictions.
- *On November 3, 2008*, Medgenics announced encouraging preliminary data in its Phase I/II clinical trial of the EPODURE Biopump for providing sustained treatment of CKD anemia. The trial is designed to assess the safety and efficacy of the EPODURE Biopump in providing sustained elevation of hemoglobin by delivering sufficient supplemental amounts of EPO for at least three to six months. Each trial participant is scheduled to be monitored for six months after the EPODURE implantation. The Company expected to continue to develop and test further applications of the Biopump platform technology from 2009 onward. Greater details of the initial results in this ongoing Phase I/II clinical trial are presented on page 6 of this update.
- *On September 24, 2008*, Medgenics announced its half-yearly report for the six-month period ended June 30, 2008. The Company reported a net loss after tax of \$2.97 million for the period, or (\$0.03) per share, versus \$1.04 million, or (\$0.02) per share, for the same period of 2007, primarily as a result of preparations for and initiation of the Phase I/II clinical trial of EPODURE, including the set-up costs associated with the new laboratories and the recruitment of additional research and development (R&D) staff. R&D costs for the six-month period were \$1.63 million versus \$0.44 million for the year-ago period, and general and administrative costs were \$1.39 million versus \$0.64 million for the first six months of 2007. Cash, cash equivalents, and short-term investments at June 30, 2008, were \$1.74 million versus \$4.68 million at December 31, 2007.
- *On July 30, 2008*, the Company announced that it received approval from Israel's Ministry of Health (MOH) to commence its Phase I/II safety and efficacy trial of the EPODURE Biopump in CKD patients. For the preceding year, Medgenics' primary focus had been to prepare for this key clinical trial, as the study may be able to not only demonstrate the safety and efficacy of EPODURE at treating anemic patients but also to validate the concept of the Biopump platform technology as an innovative approach to treating chronic diseases.
- *On June 18, 2008*, the Company announced its first full-year results since the admission of its shares to trading on the AIM. The Annual Report and Accounts of the Company and its subsidiary (the Group) for the year ended December 31, 2007, are available on Medgenics' website.

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- *On May 7, 2008*, the Company announced that it appointed Dr. Ehud Shoshani as its vice president of clinical affairs. Dr. Shoshani manages the Company's Phase I/II clinical trials with EPODURE. His 13 years of experience managing clinical trials includes a former position as chief executive officer (CEO), medical director, and head of clinical operations of Quintiles Israel (part of Quintiles Transnational Corp.), an international contract research organization. In addition, he has served as medical director at Omrix Biopharmaceuticals (now part of Ethicon, Inc.) and at Gamida Cell Ltd., a stem cell therapy company. Dr. Shoshani was awarded an M.D. in 1978 from the Technion Medical School in Haifa, Israel, and spent the next 16 years specializing in pediatrics, pediatric oncology, and hematology before entering industry.
  - *On April 14, 2008*, Medgenics provided an update on progress toward the start of its Phase I/II clinical trial with EPODURE. The Company reported that it continued to make excellent progress with its preparations to commence Phase I/II trials of EPODURE and remained confident that it would begin these trials by mid-2008 as planned. In addition, Medgenics expected to obtain the key initial safety and proof-of-efficacy data for EPODURE within three to five months after the trial commenced.

Medgenics' application for approval of the trial paralleled the Company's achievement of several important milestones, which were crucial to allow the trial to begin, as summarized below.

- The successful manufacture of the key "gutless" adenoviral vector in a Good Manufacturing Practice (GMP) vector production facility. This vector was used to prepare EPODURE Biopumps from human dermis micro-organs (MOs) to produce sufficient daily amounts of EPO to meet the Company's requirements for use in the trial.
  - The completion of the design, fabrication, and evaluation of the key proprietary devices used for harvesting patient MOs and implanting Biopumps, including EPODURE, back into patients.
  - The recruitment of key additional scientific and engineering personnel.
  - The relocation of the Group's operations to a new facility on the Teradion Business Park in Misgav, Israel.
- *On March 18, 2008*, the Company completed its move to a new facility on the Teradion Business Park in Misgav. The new facility brought together Medgenics' corporate operations with larger R&D laboratories on one site. At the same time, the Company more than doubled its scientific and engineering staff in accordance with its plan and preparation for the EPODURE clinical trial. Medgenics' new mailing address is located on page 1 of this update.
  - *On February 1, 2008*, Medgenics announced the immediate appointment of Lord Leonard Steinberg as a non-executive director on the Company's Board of Directors. A Life Peer and active member of the House of Lords in the UK, Lord Steinberg is the founder, former chairman, and life president of Genting Stanley plc (formerly Stanley Leisure plc). Stanley Leisure plc was acquired for a consideration of £639 million in 2006 by Genting International Investment (UK) Ltd, part of the Malaysian group Genting Berhad (listed on the Bursa Malaysia Securities Berhad). At the time of the acquisition, Stanley Leisure plc was the largest casino operator in the UK, owning 45 casinos, four of which were in London and 41 throughout the rest of the UK. In 1997 and 1998, Lord Steinberg received awards for North West Business Person of the Year, and in July 1999, he was awarded an Honorary Doctorate by the University of Salford. He also sits on many charitable committees, including Crimestoppers Trust.
  - *On December 4, 2007*, the Company announced that its issued shares of Common Stock of par value of US\$0.0001 each were admitted to trading on the Alternative Investment Market (AIM) of the London Stock Exchange (LSE), and dealings in the Common Shares of the Company began on December 4, 2007.
  - *On November 29, 2007*, Medgenics announced that it raised £3.28 million (\$6.72 million) in its initial public offering (IPO) in connection with its admission to the AIM market. The shares placed in the IPO were issued at 10 pence per share, which gave the Company a market capitalization of approximately £10.4 million immediately after the IPO.

## Company Background

Presented in U.S. dollars, unless otherwise noted.

Medgenics Inc. (“Medgenics” or “the Company”) is a clinical-stage biopharmaceutical company developing a novel sustained-action therapeutic protein delivery technology for the treatment of a range of chronic 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 is a protein production plant within the patient. Medgenics currently has two products in development based on its Biopump platform technology: (1) EPODURE producing erythropoietin (EPO) to treat anemia; and (2) INFRADURE utilizing interferon-alpha (IFN- $\alpha$ ) to treat hepatitis C.

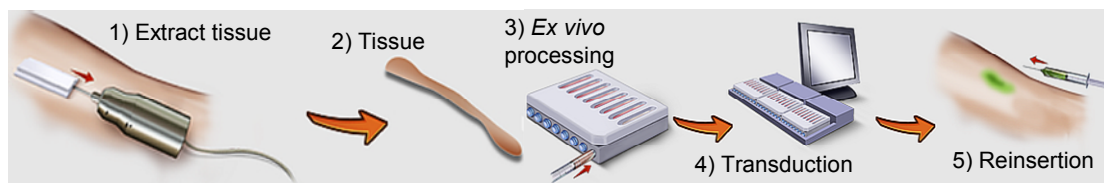
In addition, Biopump technology has the potential to be developed to produce and deliver protein therapies to treat other chronic diseases, such as multiple sclerosis using IFN- $\beta$ , hemophilia using Factor VIII, and types of growth failures and muscular atrophy using human growth hormone (hGH).

### Medgenics’ Technology

The Company’s Biopump platform technology works by using a specialized, proprietary harvesting device to remove a micro-organ (MO)—a sliver of dermal tissue—from the dermal layer of the patient’s skin using a local anesthetic. The MO is inserted into a self-standing *ex vivo* processing station, which transforms the MO into a tested Biopump within 10 to 14 days. The processing station uses a viral or non-viral vector that has been engineered to carry the gene that codes for the desired therapeutic protein but does 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 three to six months. This compares to just a few days or a week for most 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.

Figure 1  
Medgenics Inc.

#### STAGES OF THE BIOPUMP PROCEDURE



Source: Medgenics Inc.

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 of Crystal Research Associates’ Executive Informational Overview<sup>®</sup> [EIO<sup>®</sup>] on Medgenics, dated October 16, 2006, and available at [www.crystalra.com](http://www.crystalra.com)). In this manner, each patient’s MO 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 cassettes. In addition, using a technique called cryopreservation, Medgenics is able to freeze and store each patient’s MOs at very low temperatures to maintain viability

for extended periods of time. Thus, for example, the Company can remove sufficient MOs to treat the patient for an entire year or more with only one procedure.

Reinsertion 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 standard laser ablation methods or by surgical removal.

#### *Short-action Biopump*

In 2003, Medgenics' Phase I clinical proof-of-principle trial for its Biopump technology demonstrated that a short-action version of the Biopump could provide 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 of the EIO<sup>®</sup> 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 (the Harvester, Planter, Ablator, and Bioreactor).

#### *Sustained-action Biopump*

The Company's next-generation, sustained-action Biopump is designed to provide at least three 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 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- $\alpha$  (INFRADURE) in such mice.

As presented in greater detail on page 6 of this update, Medgenics' ongoing human clinical trial program aims to evaluate the safety and efficacy of EPODURE (a sustained-action Biopump EPO) for use in treating anemia. The Company also aims to enter human clinical trials in 2010 for INFRADURE (a sustained-action Biopump IFN- $\alpha$ ) to treat hepatitis C.

### **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 to 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 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 that the U.S. CKD population alone exceeds 26 million people. In addition, people with hypertension and diabetes are at an increased risk for CKD and, subsequently, anemia.

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. Conventional 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 their anemia being undertreated but also in patients who become 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 three 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 and ESRD, though it may also be used to treat anemia due to cancer, AIDS, or other indications.

#### Ongoing Phase I/II Clinical Trial of the EPODURE Biopump

As overviewed under Short-action Biopump on page 5 of this update, the Company has already demonstrated clinical proof of principle of the Biopump treatment procedure using a short-acting version of EPODURE in anemic patients. Additionally, Medgenics has proved that it can successfully manufacture the key "gutless" adenoviral vector in a GMP vector production facility—a significant achievement for the Company from a technological standpoint. A gutless adenoviral vector does not contain viral genes, thus it is prevented from producing the viral proteins that cause immune rejection. After thorough testing of the vector, Medgenics began using it to prepare EPODURE Biopumps capable of producing sufficient daily amounts of EPO to meet the Company's requirements for use in a clinical trial. The Company also completed the design, fabrication, and evaluation of the key proprietary devices required for harvesting patient MOs and implanting Biopumps, including EPODURE, back into the patient.

As such, in July 2008, Israel's Ministry of Health approved a Phase I/II clinical trial to evaluate the safety and efficacy of a long-acting version of EPODURE in patients with CKD anemia. Medgenics initiated the Phase I/II clinical trial in August 2008. The trial aims to establish that EPODURE can produce and deliver a steady therapeutic dose of EPO for at least three to six months and is currently ongoing at Hadassah Hebrew University Hospital in Jerusalem, Israel, with plans to enroll up to 30 patients by the end of 2009. Initial results of this Phase I/II clinical trial were presented during the American Society of Nephrologists' Renal Week 2008, which was held November 4-9, 2008, in Philadelphia, Pennsylvania.

In February 2009, the Company released positive data from the Phase I/II clinical trial indicating that the EPODURE Biopump successfully demonstrated safety and efficacy for the sustained protein therapy of anemia in most patients with CKD. These interim results were collected from the trial's participants thus far, who each received the lowest dose in the study: 18 to 25 IU/kg/day. Doses are scheduled to escalate to 40 and 60 units after an interim review of the trial confirms initial safety of the lowest dose in at least six participants. By February 2009, the Institutional Review Board (IRB) of Hadassah Hebrew University Hospital in Jerusalem, Israel, where the study is being conducted, had reviewed the results for the first group of low-dose patients and confirmed the safety and efficacy of EPODURE at the low dose. As such, the IRB approved continued recruitment and treatment of patients using higher EPODURE doses.

Even with the low dose of EPODURE, hemoglobin levels in most of the trial's participants to date had remained within the target range indicated by U.S. Food and Drug Administration (FDA) guidelines for the treatment of CKD anemia, which is between 10 and 12 grams per deciliter. Of the six patients dosed by February 2009, five individuals had been implanted with EPODURE for over a month. Furthermore, the first two patients enrolled in the trial have experienced over four months of EPODURE. To achieve the 18 to 25 IU/kg/day dose level in the first two patients dosed in the trial, one patient was implanted with two Biopumps and the other patient received three. Data released to date has illustrated that a one-time administration of low-dose EPODURE was sufficient to sustain therapeutic elevation of hemoglobin within the target range to treat anemia in these two patients for four months without any other EPO injections. By contrast, in standard practice today, EPO injections may be required up to several times per week, and the comparable low dose is not believed to result in sufficient hemoglobin levels in most patients.

Moreover, no adverse effects have been reported except for minor localized bruising, which is typically associated with skin biopsies and implants. Medgenics believes that it is important that no immunogenicity issues have been reported thus far in the trial, which indicates that the patients' natural immune responses have not halted the Biopump's protein production. Immunogenicity is thought to have curtailed the duration of EPO delivery in the Company's previous Phase I trials in 2003.

The trial's interim results support the Company's belief that the EPODURE Biopump can be an effective long-term treatment for anemia. Medgenics is aware of no other anemia therapy that has demonstrated maintenance of hemoglobin levels for months from a single treatment.

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## 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 200 million chronic carriers, with several 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- $\alpha$ , 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- $\alpha$  has a short half-life, requiring two to three repeat injections per week, with each injection resulting in a temporary overdose of IFN- $\alpha$ . These often cause debilitating flu-like symptoms or more serious side effects, such as depression and reduced white cell count, among others.

A PEGylated version of IFN- $\alpha$ , peginterferon- $\alpha$  (PEG-IFN- $\alpha$ ), only requires weekly injections. This type of formulation contains polyethylene glycol (PEG) to help the interferon stay in the patient's body longer. Even with PEG-IFN- $\alpha$ , a significant number of patients simply cannot tolerate the side effects. It is estimated that 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- $\alpha$ , 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 three to six months of sustained-action IFN- $\alpha$  therapy from a single treatment using the Biopump platform technology to treat hepatitis C initially and potentially other indications in the future. As noted on page 5 under Sustained-Action Biopump, the Company has reproducibly produced several months of active protein at equivalent to therapeutic levels *in vitro* as well as has demonstrated that INFRADURE Biopumps can express IFN- $\alpha$  *in vivo* in SCID mice.

Published studies have shown that steady delivery of IFN- $\alpha$  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- $\alpha$ , could be an effective way to administer IFN- $\alpha$  therapy with far fewer side effects, offering a potentially significant advancement for all hepatitis C therapies and addressing the unmet need. Medgenics anticipates initiating a clinical trial of INFRADURE in 2010.

## Protein Therapeutic Market

The protein therapeutic market was valued at over \$57 billion in 2006 and was forecast to reach \$87 billion by 2010, due to heavy demand and rapid sales in the U.S. and Europe (Sources: RNCOS 2007 and Kalorama Information 2006). Further estimates of this market predict a compound annual growth rate of 12.83% until 2010, with the U.S. remaining the largest market for therapeutic proteins followed by Europe and Japan. In 2006, patients received roughly \$11.9 billion worth of EPO injections to treat anemia. Patients treated with IFN- $\alpha$  for hepatitis C and some forms of cancer composed a \$3.5 billion market in 2005.

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 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 toward 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' long-term strategy to enter this market is to develop a strategic alliance with a major partner in order to proceed with further clinical trials, regulatory approvals, and commercialization of EPODURE and other applications of the Biopump platform technology. To this extent, the Company has initiated discussions with several potential strategic partners.

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 of the EIO<sup>®</sup>.

### **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. The Company also has a wholly owned subsidiary (Medgenics Medical Israel Ltd.) and major operations in Misgav, Israel. Medgenics moved its operations from Karmiel, Israel, to the facility in the Teradion Business Park in Misgav in March 2008. In doing so, the Company was able to bring all operations under one roof, which represented an important step for enhancing communication among the various departments. Medgenics' U.S. location is in Vienna, Virginia.

Medgenics employs 18 individuals, comprising three Ph.D.s, one M.D., and nine scientists and engineers, among others. The Company 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 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 of the EIO<sup>®</sup>. In addition, the Company has recently made new appointments to its leadership team, including Dr. Ehud Shoshani as vice president of clinical affairs and Lord Leonard Steinberg as non-executive director on the Board of Directors. Dr. Shoshani has 13 years of experience managing clinical trials, and Lord Steinberg is a respected businessman in the UK, with substantial experience in the London stock market.

Since May 2006, the Company has developed the first versions of its sustained-action Biopumps intended to treat anemia and chronic hepatitis C, moved its EPODURE Biopump into a Phase I/II clinical trial, raised £3.28 million (\$6.72 million) in an initial public offering (IPO), and began operating as a publicly traded company through admittance to the London Stock Exchange's (LSE) Alternative Investment Market (AIM) in December 2007. Medgenics also recently completed a Warrant exercise program through which \$430,000 was invested in the Company. Medgenics trades under the symbols MEDG (restricted securities under U.S. securities laws) and MEDU (unrestricted shares).

## Key Points to Consider

Presented in U.S. dollars, unless otherwise noted.

- **The Biopump Platform Technology.** Medgenics' Biopump platform converts a sliver of a patient's own dermal tissue into an internal protein production plant through *ex vivo* transduction with a viral vector and reinsertion 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: (1) EPODURE providing erythropoietin (EPO) to treat anemia; and (2) INFRADURE providing interferon-alpha (IFN- $\alpha$ ) to treat hepatitis C.
- **Results Published in Key Journals.** The Company's research has been published in *Blood*, the *Journal of the American Society of Hematology*, and *Molecular Therapy*, a journal by the American Society of Gene Therapy. In addition, initial results of the current Phase I/II clinical trial have been presented at the American Society of Nephrologists' Renal Week 2008, the largest nephrology meeting of its kind. Renal Week 2008 provided a forum for 11,000 nephrologists to discuss the latest findings in renal research as well as hold educational sessions related to advances in renal care.
- **Sustained-Action Biopumps.** Medgenics' Biopumps have reproducibly shown months of sustained production of active EPO and IFN- $\alpha$  in laboratory and mice testing using a new vector with non-immunogenic properties (a "gutless" adenoviral 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 moved a sustained-action Biopump (EPODURE) into a Phase I/II clinical trial in August 2008.
- **Initial Phase I/II Trial Data.** In February 2009, the Company released interim data collected from the first six participants in EPODURE's Phase I/II clinical trial and most patients have shown sustained hemoglobin levels that remained within the target range to treat anemia for over a month. Moreover, the data illustrated that hemoglobin levels in the first two participants rose and remained within the target range to treat their anemia for at least four months, with no reports of serious adverse effects. In particular, Medgenics believes that the lack of immunogenicity issues thus far in the trial indicates that the patients' natural immune responses have not halted the Biopump's protein production.
- **Market Opportunities.** Medgenics' Biopump technology addresses the majority of the \$57 billion market (as of 2006) for protein therapeutics, aiming to replace more than \$30 billion in protein injections each year. In addition, the Company's platform technology can be applied to a range of therapeutic proteins, potentially opening new market segments.
- **Intellectual Property.** The Company's technology is protected by over 44 patents and patent applications in the U.S. and worldwide, including a patent issued in December 2008 covering critical claims of the Biopump platform technology in the U.S.—Medgenics' largest target market.
- **Management.** Medgenics' team is experienced in biotechnology and biomedical devices as well as the healthcare, finance, medical, and academic communities. The Board of Directors comprises current and former directors of global healthcare companies, and the Scientific Advisory Board includes past presidents of the American Gastroenterological Association, the American Society of Renal Physicians, and the American Society of Gene Therapy. New members include Dr. Shoshani, vice president of clinical affairs, and Lord Steinberg, non-executive director on the Board of Directors.
- **Initial Public Offering (IPO).** Medgenics raised £3.28 million (\$6.72 million) in an IPO in December 2007 and began operating as a publicly traded company on the London Stock Exchange's (LSE) Alternative Investment Market (AIM) in December 2007.
- **Cash Position.** Medgenics recently completed a Warrant exercise program through which \$430,000 was invested in the Company. Medgenics also continues to receive ongoing government funding from Israel's Office of the Chief Scientist and is in the process of raising further funds to support its ongoing clinical trial, development, and testing of the Biopump platform and associated products.

## Risks

Some of the information in this Quarterly Update relates to future events or future business and financial performance. Such statements can only be predictions and the actual events or results may differ from those discussed due to the risks described in Medgenics' statements filed to the AIM, as well as other forms filed from time to time. The content of this update with respect to Medgenics has been compiled primarily from information available to the public released by Medgenics through news releases, annual and interim financial reports, and AIM filings. Medgenics is solely responsible for the accuracy of this information. Information as to other companies has been prepared from publicly available information and has not been independently verified by Medgenics. Certain summaries of activities have been condensed to aid the reader in gaining a general understanding. For more complete information about Medgenics, please refer to the Company's website at [www.medgenics.com](http://www.medgenics.com). Additionally, please refer to Crystal Research Associates' base report, the Executive Informational Overview<sup>®</sup> (EIO<sup>®</sup>) dated October 16, 2006, and located on Crystal Research Associates' website at [www.crystalra.com](http://www.crystalra.com) for more comprehensive details of Medgenics' risk factors.

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# Crystal Research

a s s o c i a t e s

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