Ischemic stroke is caused by a blockage in a blood vessel that stops the flow of blood and deprives the surrounding brain tissue of oxygen.

Without oxygen, the brain cells in the immediate area begin to die and release a cascade of toxic chemicals that threaten brain tissue in the surrounding area: the ischemic penumbra.

The main goal in treating acute ischemic stroke is to preserve healthy brain tissue surrounding the blockage.

This can be accomplished by removing the blockage and restoring blood flow to the area, or by protecting the surrounding tissue.

According to the Stroke Center at Newark, New Jersey’s University Hospital, thrombolytic drug therapy has helped to change the course of ischemic stroke.

A thrombolytic drug, also called a fibronolytic or clot-buster, is delivered through the blood vessels to break-up the clot that is disrupting the blood flow.

The FDA has approved only one thrombolytic agent: tissue Plasminogen Activator (tPA), for treating acute ischemic stroke.

Stroke specialists use a genetically engineered version first used to treat blood clots in the heart.

Use of tPA offers a 30 percent to 50 percent better chance of cure from stroke disability, according to physicians.

But a Canadian company, Calgary, Alberta-based Stem Cell

(Continued on page 2)
Therapeutics Corp. (CA: SSS), is working on a treatment for acute ischemic stroke that stimulates creation of new nerve cells to replace cells destroyed or damaged.

If such a treatment works, wouldn’t it have an enormous leg up on the competition?

Company CEO Alan Moore told Stem Cell Business News that, barring unforeseen circumstances, his company may have a unique entry point into a potential $3 billion market within five years.

Believable? Sure. We’re not talking basic research here. We’re talking clinical trials using human patients.

On May 28 the company said it had enrolled the first such patient in its Regenesis Phase IIB stroke trial testing the new treatment.

The trial is a double-blind, randomized, placebo-controlled Phase IIB clinical trial for SCT’s lead program, NTx-265, for the treatment of AIS.

NTx-265 is a therapeutic regimen of two approved and clinically well-defined drugs: human Chorionic Gonadotropin (hCG) and Erythropoietin (EPO), targeting the treatment of stroke.

The twin objectives of the regimen are to stimulate the growth and differentiation of new neurons to replace the brain cells that were lost or damaged by the stroke, and importantly, to direct motor, visual and cognitive recovery after AIS.

The first patient was enrolled by three physicians: Judith Jarrett, Dr. Gordon Gubitz, and Dr. Stephen Phillips at the Queen Elizabeth II Health Sciences Centre in Halifax, NS.

Co-lead investigators for the Regenesis Phase IIB trial are Dr. Steven C. Cramer, principal investigator of the BETAS Phase IIa stroke trial, at the University of California, Irvine; and Dr. Michael Hill at the Foothills Hospital at the University of Calgary.

The Regenesis Phase IIB stroke trial will be a multi-site trial projected to enroll 134 patients at approximately 18 Canadian sites.

A similar U.S. Phase IIB acute ischemic stroke trial was recently approved by the U.S. Food and Drug Administration and is projected to enroll 20-30 patients at 3-4 enrolling U.S. sites.

The Canadian and U.S. Phase IIB clinical stroke studies share similar protocols, safety and efficacy endpoints.

“This is an exciting time for the company as we continue to advance our lead program in stroke,” said SCT’s Dr. Allen Davidoff in a statement. “We hope the Regenesis Phase IIB trial will build upon the promising results from the BETAS Phase IIa trial by demonstrating the positive effect that NTx-265 exerts on recovery of visual, motor and cognitive recovery in patients who have suffered moderate to severe acute ischemic stroke. We anticipate completing enrollment of the Regenesis study by the end of 2008.”

Animal studies have shown a significant recovery in motor function after receiving the NTx-265 regimen 24-48 hours post stroke.

Encouraging clinical results in SCT’s BE-
TAS Phase IIa stroke trial were presented at the International Stroke Conference in February 2008, showing clinically relevant recovery in 8 of 8 patients who received the complete regimen.

SCT is recruiting patients for the multicentre, double-blind, placebo-controlled Regenesis Phase IIIB stroke study for NTx-265 with primary endpoints of efficacy.

Patient enrollment is expected to be complete by the end of 2008 with top-line efficacy data expected to be released before the end of the first quarter of 2009.

Q&A: Alan Moore

[Editor’s Note: Our editors asked Stem Cell Therapeutics CEO Dr. Alan Moore about NTx-265 and its impact on stroke and the company’s future. Below are Dr. Moore’s responses.]

What is the relationship, if any, between administration of NTx-265 after a stroke, and administration of a thrombolytic drug (i.e., tissue Plasminogen Activator, tPA)?

Moore: NTx-265 can be used whether or not tPA has been given, as long as the patients still meet the study entry criteria.

How soon after a stroke would you expect NTx-265 to be administered for optimum outcomes?

Moore: In the Regenesis protocol, NTx-265 therapy is begun 24 to 48 hrs. post-stroke. Animal data suggest, however, that the window of opportunity may eventually be even greater, perhaps up to seven days post-stroke.

Do you have any figures estimating the potential market size for NTx-265 for acute ischemic stroke?

Moore: Risk adjusted net present value (NPV) for NTx-265 is approximately US$3 billion.

Whom do you see as your main competitor(s) in this space, if any?

Moore: No one, really. All of the current in-development therapies have an initial window within the first nine hours, none of which would prevent NTx-265 from also being used, if needed.

Assuming the trials are all successful, when might you expect to have a marketable product?

Moore: If a full, large Phase III program is required, then [I would predict] 2013 in the United States, and [I would predict] a year later worldwide. However, given that the NTx-265 regimen comprises two already marketed drugs, it is possible that we could be allowed a smaller and hence faster program.

Stem Cell Therapeutics is developing drug-based therapies to treat central nervous system diseases.

Contact: http://www.stemcellthera.com

Preclinical Trials

Israeli Firm’s Cells Show “Significant Advantage” In Pre-Clinical Parkinson’s Study

Parkinson’s disease, which belongs to a group of conditions called movement disorders, has four main symptoms: tremor, or trembling in hands, arms, legs, jaw, or head; rigidity, or stiffness of the limbs and trunk; bradykinesia, or slowness of movement; and postural instability, or impaired balance.

These symptoms usually begin gradually and worsen with time.

As they become more pronounced, patients may have difficulty walking, talking, or completing other simple tasks.

Parkinson’s is both chronic, meaning it

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improvement in NTF rats’ motor functions, in compared to the mesenchymal cell group and the controls.

Moreover, the NTF cells increased the level of the neurotransmitter dopamine.

Low levels of dopamine cause Parkinson’s.

The researchers also detected, 45 days post-transplantation, viable transplanted cells which migrated toward the impaired portion of the affected brain.

The company believes that this is evidence of the integration ability of BrainStorm’s cells in the damaged brain.

This is the second study completed using BrainStorm’s cells that produced similar results.

The findings of the study were presented by Offen at a stem cell meeting in Tel-Aviv in conjunction with the ILSI-Biomed Israel 2008 Conference.

“These exciting results provide validation of our previous scientific work,” said Prof. Eldad Melamed, chairman of the company’s scientific advisory board and the company’s chief medical advisor. “The study indicates that our cells show survival, integration and clinical efficacy. When considering the advantages of using adult stem cells, which are easy to harvest, autologous, do not create tumor problem and do not present the moral/religious issues that are often discussed with embryonic stem cells, we remain optimistic that we will soon be able to embark on clinical trials in Parkinson’s disease.”

The researchers worked with the 6OHDA rat model for Parkinson’s disease because it is considered the most dependable animal model for testing potential treatments.

In the study, BrainStorm said it encountered some immune rejection problems, but overall its cells showed survival, integration, and efficacy.

It is expected that human trials will use autologous NTF cells, which should have fewer or no immune rejection problems.

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Market Potential

BrainStorm is developing several adult stem cell therapeutics derived from autologous (self) bone marrow cells for the treatment of neurodegenerative diseases.

The company’s initial focus is on Parkinson’s, amyotrophic lateral sclerosis (ALS, or Lou Gehrig’s disease), and spinal cord injury.

The company believes its technology also has promise for treating several others diseases and disorders, including multiple sclerosis, Huntington’s disease, and stroke.

In the area of Parkinson’s disease, the market for BrainStorm’s NTF cells includes the four million Parkinson’s patients around the world, 1.5 million of whom are in the United States.

According to BrainStorm, global sales of current Parkinson’s therapeutics in 2006 were $3 billion, an increase of 11 percent from 2005.

Revenues of the only approved Parkinson’s drugs, which treat the symptoms of the disease, across the major markets (United States, Japan, France, Germany, Italy, Spain, and the UK) totaled more than $2.2 billion in 2006.

Revenues from Parkinson’s therapeutics are expected to exceed $4.6 billion by 2012.

But BrainStorm’s approach is obviously not the treatment of Parkinson’s symptoms, but the treatment of the core problem – namely, the death of dopaminergic neurons.

That makes every Parkinson’s patient a potential client, the company says.

In addition, it appears that BrainStorm is the only company using adult stem cells to target Parkinson’s.

In the ALS space, the company may be moving toward clinical trials in Israel sometime this year.

The NurOwn patent pending technology is based on discoveries made by the scientific team led by neurologist Melamed, head of neurology at Rabin Medical Center, and expert cell biologist Dr. Offen, head of the neuroscience laboratory at the Felsenstein Medical Research Center of Tel-Aviv University.

The technology allows for the differentiation of bone marrow-derived stem cells into functional neurons and astrocytes, as demonstrated in animal models.

The company holds rights to develop and commercialize the technology through an exclusive, worldwide licensing agreement with Ramot at Tel Aviv University Ltd., the technology transfer company of Tel-Aviv University.

Contact: http://www.brainstorm-cell.com

Ischemia Patients In Stem Cell Protocol Experience Significant Improvement

TCA Cellular Therapy (Covington, La.) on May 29 said participants in a Food & Drug Administration (FDA) protocol using the company’s stem cells to treat lower limb ischemia are experiencing increased mobility and decreased pain in lower legs.

Lower limb ischemia is a condition where plaque build-up causes decreased circulation in the lower leg.

Symptoms of the condition include intense pain and swelling.

Study participants may have had different factors that contributed to their condition: a family history of Peripheral Artery Disease (PAD), history of smoking and other vascular conditions.

Common among them, however, were that more traditional treatments (i.e., stents and grafts) were ineffectual and that the patients could not continue their daily activities.

One patient was an avid gardener before she had to give up the hobby last year.

She could no longer walk the length of the lawn without stopping to rest her throbbing legs.

“It got to the point where the intervals of rest were not even enough to ease the pain,” she said.

The study participants were referred by their vascular surgeons to TCA Cellular Therapy, where Gabriel Lasala, M.D., and Jose Minguell,
Preclinical Milestone In Congestive Heart Failure Research

Mississauga, Ont.-based Covalon Technologies Ltd. (CA:COV) said on May 28 that it has achieved a preclinical milestone in its research project to identify a way to stimulate new blood vessel growth and regeneration of tissues damaged by loss of, or restricted blood flow due to congestive heart failure, diabetes, chronic wounds, peripheral vascular disease and other conditions.

According to the company, the EPAS-1 research project will allow Covalon to produce “universal donor” mesenchymal stem cells that can be used by all individuals for myocardial preservation by therapeutic cell transplantation following loss of blood flow due to coronary vessel occlusion.

The use of a “universal donor” will allow for simplification and standardization of procedures related to stem cell therapy including cardiovascular disease and generally in regenerative medicine.

“Covalon’s cell therapy program is designed to generate mesenchymal stem cells (EPAS1-cells) that express genes that control the production of growth factors at the site of cell transplantation that may be useful for new blood vessel formation, maturation and tissue regeneration,” said CEO Dr. Frank DiCosmo.

“The market opportunity for EPAS-1 is huge,” said chief business officer William Jack-

(Continued on page 7)
In industrialized countries, the prevalence of cardiovascular disease is related to an increasingly unhealthy lifestyle, with risk factors such as lack of exercise, a fatty diet, obesity and smoking. These risk factors are also linked to diabetes that is associated with an increased risk of developing heart disease.

There are approximately 20 million diabetics in the United States alone.

In recently completed preclinical studies, swine stem cells derived from the marrow of a single donor animal with blood group “O” could be readily isolated, genetically manipulated with EPAS1, frozen and thawed for use.

Various dosages of mesenchymal stem cells, greater than 90 percent viability, prior to injection, could be introduced into the myocardium of eight recipient swine seven days post-myocardial infarction; surviving cells could be readily identified two weeks post-implantation.

Mesenchymal stem cells altered with the EPAS1 gene showed significantly enhanced production and secretion in vitro of several important protein factors that are essential to new blood vessel growth (angiogenic) and further maturation.

Direct introduction of genetically engineered EPAS1 cells by intra-cardiac injection into the hearts of swines showed no significant, adverse side-effects.

In vivo, mesenchymal stem cells altered with the EPAS1 gene initiated an enhanced host-derived angiogenic response over that of non-EPAS1 modified mesenchymal stem cells.

EPAS1 over-expression and the various proteins under control of the EPAS1 gene, enhances the cellular regenerative properties of mesenchymal stem cells by inducing secretion of certain protein factors that are essential to robust angiogenesis and functional maturation.

EPAS1 is mainly expressed in vascular endothelial cells, that are essential to new blood vessel growth and appears to drive a superior angiogenic response with enhanced stability of the resultant vessels.

The overall significance is that mesenchymal stem cells can be readily isolated, grown to useful dosages and manipulated genetically to express EPAS1 for therapeutic application in damaged heart tissue.

Covalon’s approach is intended to improve the function of damaged tissue, rather than merely address the symptoms of the disease.

EPAS1 cell therapy is intended to enhance the beating of the damaged heart tissue with a cell therapy that delivers mesenchymal stem cells loaded with the EPAS1 gene that controls the production of many essential blood vessel growth factors.

The system is expected to improve blood flow and oxygen delivery to the damaged heart by stimulating the growth of new blood vessels, by a process of therapeutic angiogenesis.

Porcine myocardial studies were performed off-site by an independent research organization under contract to Covalon, and mesenchymal stem cells preparation, gene enhancement and characterization were conducted by Dr. Jacques Galipeau, M.D., associate professor of medicine and oncology at the Sir Mortimer B. Davis Jewish General Hospital (McGill University).

The need for improved methods to repair and regenerate tissue has fueled the development of many innovative technologies in the wound care market.

The convergence of pharmaceutical, medical device, and biotechnology companies have both altered and shaped the market in the hard-to-heal wound industry.

Advanced-technology bio-engineered products that actively stimulate and/or integrate with wound milieu and tissues to promote faster wound healing are increasingly being sought after.

Active wound care products show an added advantage over the traditional dressings in terms of healing rate by providing and promoting an environment conducive to rapid wound healing.

These technologies will address unmet clinical needs of an aging population, as well as improve patient outcome in a wide range of medi-
Covalon develops interactive wound care products that are intended to actively support the healing of wounds and regeneration of tissues through processes that interact either directly or indirectly with the damaged area.

The current products in distribution and the processes under development are far more advanced than traditional wound care treatments, and consist of collagen-based materials and platforms, as well as bioactive, molecular coatings for implantable medical devices.

Interactive wound care products can serve as temporary coverage for a wound designed to stimulate improved tissue repair.

The components of these products may include growth factors and enzyme inhibitors to cellular “allogenic” or universal donor mesenchymal stem cells, engineered to carry the EPAS1 gene and induce angiogenesis at the site of cellular deposition, or such cells can be adhered to and delivered via a collagen-based scaffold.

The target markets for such products include chronic and acute wounds, burn wounds and regenerative medicine.

Covalon’s EPAS1 platform is intended to deliver precursor cells loaded with the EPAS1 gene that is expected to induce therapeutic angiogenesis and blood flow to ischemic tissues.

Contact: http://www.covalon.com

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**Medical School To Study CellCyte’s Heart Attack Product Candidate**

Bothell, Wash.-based CellCyte Genetics Corporation (CCYG) said on May 28 it will work with Northwestern University’s Feinberg School of Medicine (Chicago, Ill.) to perform an acute myocardial infarction (AMI) disease model study in mice using the company’s CCG-TH30 product candidate.

The goal of the study is to evaluate the functional benefit of the CCG-TH30 therapy in a disease model outcome study representative of the AMI (heart attack) indication.

CCG-TH30 is a modified form of the human glycoprotein that CellCyte is evaluating as its lead product candidate.

The product is designed to send autologous bone marrow-derived (adult) stem cells to the heart of patients after a heart attack.

Douglas W. Losordo, M.D., director of Feinberg Cardiovascular Research Institute, will serve as the principal investigator on the study.

“This is another important collaboration for our program, as it allows us to evaluate the functional outcome benefit of the CCG-TH30 therapy as compared to standard cell therapies where delivery agents aren’t used,” said CSO Ronald W. Berninger.

Losordo is a cardiologist at Northwestern Memorial Hospital and is the director of Cardiovascular Regenerative Medicine and the Feinberg Cardiovascular Research Institute, both at Northwestern Memorial Hospital.

**Washington University Study On Glycoprotein Products**

In related news, on June 3 the company said it had selected the Cardiovascular Phenotyping Core at Washington University School of Medicine in St. Louis to perform a study in mice to further evaluate CellCyte’s glycoprotein products.

The goal of the study is to investigate the efficiency of CellCyte’s glycoprotein products in a preclinical model of myocardial infarction (heart attack).

The glycoprotein platform comprises both natural and modified versions of a human glycoprotein, which is the technology CellCyte licensed from the Department of Veteran Affairs, the company told Stem Cell Business News.

CellCyte Genetics is developing stem cell enabling therapeutic products designed to allow more efficient delivery and increased retention of adult stem cells to diseased organs, such as the heart.

Contact: http://www.cellcyte.com

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Business Briefs

StemCells Awarded Patent Related To Use Of Monoclonal Antibodies

Palo Alto, Calif.-based StemCells, Inc. (STEM) said on June 6 that the U.S. Patent Office has issued the company a patent claiming the use of additional monoclonal antibodies for the prospective isolation of rare cells from human neural tissue, such as the company’s HuCNS-SC product candidate (purified human neural stem cells).

StemCells is developing cell-based therapeutics to treat diseases of the central nervous system and liver.

Contact: http://www.stemcellsinc.com

Stem Cell Sciences Granted Second European “Nanog” Patent

San Francisco-based Stem Cell Sciences plc (AIM:STEM, ASX:STC) said on June 4 that the European Patent Office had granted it a second patent for Nanog, a key factor used to convert adult cells back into a pluripotent state.

With this technology, adult cells can be reprogrammed to behave like embryonic stem cells, thus avoiding the controversy associated with using embryos.

The resulting pair of patents have claims which cover manipulating expression of human and mouse Nanog, cells containing introduced human and mouse Nanog genes, reprogramming methods using human and mouse Nanog and related culture media products.

“Nanog is like a master control switch,” said chief scientific officer Dr. Tim Allsopp. “Nanog is a protein that can bind to the DNA encoding many other genes, and can regulate their pattern of activity. In effect, we can use the Nanog gene to turn back the developmental clock in cells and induce an embryonic status in which the cells have the hallmark features of indefinite growth and pluripotency in culture.”

Contact: http://www.stemcellsciences.com

National Stem Cell Holding Changes Name

Mountainside, N.J.-based National Stem Cell Holding, Inc. (OTC) said on May 28 that it is changing its name to Proteonomix, Inc.

The change will also entail a change in its trading symbol.

“Our new name reflects the fact that we are emerging out of our research and development stage and commencing the commercialization of our technologies,” CEO Michael Cohen said. “These technologies relate in great part to the identification of proteins, and their structure and functions within the emerging biotherapeutics field.”

The company intends to begin marketing its current portfolio biomarkers to research laboratories globally.

National Stem Cell Holding is focused on developing therapeutics based upon the use of human stem cells and their derivatives.

The company is developing a pipeline of

(Continued on page 10)
proprietary stem cell therapeutics with a particular focus on diabetes.

The company also has wholly-owned subsidiaries: the Sperm Bank of NY (tissue bank and IVF laboratory) and National Stem Cell Blood Laboratories Inc. (cord blood banking program), and its affiliate, Decouverte Cosmetique, Inc. (cosmetics).

Contact: http://www.nationalstemcell.com

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