Neuralstem Sues StemCells Over New Patent

Rockville, Md.-based stem cell company, Neuralstem, Inc. (CUR), said that it filed a suit on May 7 against Palo Alto, Calif.-based StemCells, Inc., saying that “StemCells intentionally withheld crucial information highly material to the patentability of StemCells’ ‘new’ patent (U.S. Patent No. 7,361,505).”

The company said that this was allegedly done “with the intent to deceive the United States Patent Office in order to get the ‘505 patent allowed.”

As a result of these actions, Neuralstem is asking for a declaratory judgment that the patent is unenforceable.

The suit was to be filed in the United States District Court for the District of Maryland Southern Division.

[Editor’s Note: Representatives of StemCells did not respond to several requests from Stem Cell Business News for comment, nor did they as of press time (May 9, 2008) issue a formal statement about the suit.]

On May 6, Neuralstem said it had filed a motion to re-open the patent infringement lawsuit with StemCells, Inc., and to have the stay lifted, so that the case can be disposed of on summary judgment as soon as possible.

“While we believe that it is clear that we are not infringing this patent, and we have not yet been directly accused by StemCells, Inc. of infringing this patent, the threatening statements in their press release of April 23 leave the misleading impression that we would require a license from them as a result of the issuance of this patent. Nothing could be further from the truth,” said Neuralstem CEO Richard Garr. “And, in addition to finding that the patent is unenforceable

(Continued on page 2)
against us, or anyone else for that matter, as a result of their actions, we are asking that the Court also declare that we are not infringing the patent and that the patent is also invalid.”

“We are confident that their intentional withholding of highly material information and their intent to deceive the Patent Office, will result in this patent being unenforceable,” Garr said.

“We are going back to court,” Garr said in a May 6 statement, “because the recent actions of the U.S. Patent Office now entitle us to summary judgment in the case. Completely contrary to the public statements made by StemCells, Inc., the Patent Office actions have destroyed the basis for the infringement suit filed by StemCells, Inc. against us. As we have stated in the filings, we are now entitled to have the litigation dismissed once and for all.”

StemCells (STEM) said on April 15 that the U.S. Patent and Trademark Office (PTO) had upheld two of the company’s neural stem cell patents, with minor amendments.

The company said the PTO’s decisions amount to a rejection of the arguments raised by Neuralstem, Inc. in its re-examination petitions of last year.

But Neuralstem, which sought PTO re-examination of the patents, issued a statement at the time saying StemCells’ announcement had “completely mischaracterized” the Patent Office’s decision.

Neuralstem said the amendments made by StemCells during the re-examination had actually nullified StemCells’ earlier claims of infringement.

The upheld patents (Nos. 5,851,832 and 6,497,872) have been exclusively licensed by the company and claim, respectively, methods for proliferating neural stem and progenitor cells and for using these cells as transplantation therapeutics.

The patents are two of four patents which are the basis of a patent infringement suit initiated by StemCells against Neuralstem in 2006.

In late 2006 and early 2007, Neuralstem petitioned the PTO to re-examine all four of the litigated patents.

Neuralstem’s patented technology enables production of neural stem cells of the human brain and spinal cord in commercial quantities, and control of the differentiation of these cells into mature, physiologically relevant human neurons and glia.

Contact: http://www.neuralstem.com

(Continued on page 3)
Critical Limb Ischemia: Harvest Technologies Has Cause For Optimism

New Stem Cell Treatment Is Successful In CLI Patients

Critical limb ischemia (CLI) is a severe obstruction of the arteries that seriously decreases blood flow to the hands, feet and legs, and has progressed to the point of severe pain and even skin ulcers or sores.

According to the Vascular Disease Foundation, CLI is often present in individuals with severe peripheral arterial disease (PAD).

The pain caused by CLI can wake up an individual at night.

This pain, often called "rest pain," can be relieved temporarily by hanging the leg over the bed or getting up to walk around.

Several medications may be prescribed to prevent further progression of the disease and to reduce the effect of contributing factors such as high blood pressure, high cholesterol and diabetes, and most certainly to reduce the pain.

Medications that prevent clotting or fight infections may also be prescribed.

According to the VDF, surgery and endovascular procedures such as angioplasty can be successful in restoring oxygenated blood flow.

But Plymouth, Mass.-based Harvest Technologies Corp. has what it believes is a better idea, and a new study provides some basis for optimism.

A study in Germany that treated patients with CLI (or, end-stage peripheral vascular disease) using a composition of autologous stem cells created using Harvest’s technology has reported early success.

Claas Ludermann, M.D., a specialist in vascular medicine, presented preliminary data at a meeting of the German Society of Cardiology from a clinical trial being conducted at the Berlin Vascular Center of Franziskus Hospital under the direction of Berthold Amman, M.D.

The “BONe Marrow Outcome Trial-2” (BONMOT-2) is a randomized, controlled, double-blinded study treating patients with end-stage CLI.

According to the company, this same treatment methodology has shown to be very promising in international clinical pilot studies, including a successful pilot study (BONMOT-1) of 60 patients recently completed under Amann’s supervision at the Berlin Vascular Center.

Ludermann presented results on the first 12 of 90 patients who completed the BONMOT-2 study protocol—six from the control group who received a placebo treatment, and six from the treatment group who received an injection of a concentrate of their own bone marrow stem cells.

The stem cell concentrate was produced at the point of care (concentrated at the patients’ bedside) using the Harvest Technologies BMAC System.

The treatment group showed a 100 percent improvement in perfusion (0.3 to 0.62) as measured by the ankle-brachial index (ABI) compared to the control group, which exhibited only a non-significant change in ABI (0.4 to 0.5).

Increased blood supply was also confirmed by an increase of oxygen pressure in the foot, which showed the treatment group having an 18-point increase compared to a seven-point increase in the control group.

The treatment group also showed an improvement in a standardized quality-of-life assessment over the control group, and also a significant improvement of 30 meters in pain-free walking compared to an increase of 10 meters for the control group.

“It is encouraging that the early results of the BONMOT-2 study closely mirror the positive results obtained in our pilot study,” said Ludermann. “We are optimistic that this favorable trend will continue as more study data is available.”

Contact: http://www.harvesttech.com

(Continued on page 4)
With decreased blood flow to the affected extremity, patients can suffer a host of complications, including nerve and tissue damage.

In advanced stages, limb ischemia can lead to gangrene, which often requires treatment with amputation.

The current market for therapeutics and other interventions to treat limb ischemia is estimated to be approximately $1.2 billion.

Pluristem Therapeutics Inc. is developing non-personalized (allogeneic) cell therapy products for the treatment of several severe degenerative, ischemic and autoimmune disorders.

The company is developing a pipeline of products, stored ready-to-use, that are derived from the human placenta, a non-controversial, non-embryonic, adult stem cell source.

Contact: http://www.pluristem.com

Cardiac Ischemia: Arteriocyte Hopes To Launch Phase II Trial Of Its Treatment In 4th Q

Funding Remains Biggest Challenge

Cardiac ischemia occurs when blood flow to the heart muscle (myocardium) is obstructed by a partial or complete blockage of a coronary artery.

A sudden, severe blockage may lead to a heart attack (myocardial infarction).

Cardiac ischemia may also cause a serious abnormal heart rhythm (arrhythmia), which can cause fainting or even sudden death.

Treatment is directed at improving blood flow to the heart muscle and may include: medication such as aspirin, beta blockers and nitrates; angioplasty or stent placement; and coronary artery bypass surgery.

But a significant portion of patients with chronic ischemia are not helped by the usual

(Continued on page 5)
Stem Cell Business News

Arteriocyte’s goal is to develop commercially available stem cell based therapies using multiple sources of adult derived stem cells (marrow, peripheral cord blood, and cartilage) for disease where surgical interventions are inadequate.

Contact: http://www.arteriocyte.com

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Diabetes: CureDM’s Therapy Achieves Major Development Milestone

But Stem Cell Execs See Minimal Impact On Their Plans

Wynnewood, Pa.-based CureDM, Inc., a biopharmaceutical company developing new therapies for diabetes, said on April 30 it had achieved a major drug development milestone for Human proIslet Peptide (HIP).

The company said it hypothesized that treatment with this therapeutic will restore human pancreatic function without the use of stem cells.

Two executives of companies that are developing stem cell-based therapies for diabetes told us why the HIP technology would probably have minimal impact on their plans.

CureDM’s Achievement

CureDM successfully stabilized HIP to improve its bioavailability with recent dose response studies indicating that the dosage used in man may be as much as 100-fold lower than the native form.

HIP is a 14-amino acid human peptide derived from a specific human gene responsible for populating the pancreas with islets, which contain the cells that secrete insulin and other hormones necessary to prevent diabetes.

“Meeting this milestone has a significant impact on the commercial value of Human proIslet Peptide,” said CEO Loraine V. Upham,

(Continued on page 6)
CEO. “Not only does this mean lower costs associated with the manufacture and commercialization, but also potentially better safety and tolerability outcomes in human trials.”

CureDM has filed with the FDA and anticipates approval for commencement of human studies in early 2009.

Further studies are underway to determine just how low of a dose is possible.

Previous studies have confirmed that the stabilization of HIP did not adversely affect the efficacy and demonstrated that normal glucose levels were achieved after 25 days of treatment and remained normal after the therapy was stopped.

Human proIslet Peptide (HIP) stimulates the differentiation of pancreatic progenitor cells, which are present in the adult pancreas, into new insulin-producing islets.

Each new islet contains pools of beta cells which make insulin.

The CureDM approach to restore new insulin-producing cells through islet neogenesis can potentially reverse both Type I and Type II diabetes.

Patients with Type I diabetes will require pretreatment with an immune tolerance agent to protect new islets formed by HIP.

Impact On Stem Cell-based Diabetes Research

Dr. James Musick, CEO of Vitro BioPharma (Aurora, Colo.), which has generated 29 adult human pancreatic stem cell lines, said he was not familiar with CureDM’s specific technology, but knew of other products that are similar.

He mentioned Lisofylline (a synthetic small molecule with novel anti-inflammatory properties) and INGAP (islet neogenesis-associated protein).

According to DiaKine Therapeutics (Charlottesville, Va.), Lisofylline has demonstrated that it can effectively prevent Type I diabetes in preclinical models.

“Such approaches are potentially highly beneficial since it may be possible to block autoimmunity to beta cells and stimulate endogenous regeneration from stem cells,” Dr. Musick said. “This could potentially obviate the need for islet transplantation, whether the islets are derived from donated pancreas glands or stem cells. It is imperative to block autoimmune rejection for these approaches to move forward.”

Another stem cell company working in the diabetes space is Novocell of San Diego, Calif.

Novocell is developing a renewable source of specialized cells that can be used to treat chronic cellular diseases, with an initial focus on diabetes.

Valerie Baird of Novocell said it is difficult to comment on CureDM’s technology, because it “has yet to be fully validated scientifically.

There is little doubt that replacing islets will benefit patients with Type I diabetes since the Edmonton Protocol has validated cell therapy to improve islet mass,” she said. “We have now shown that human embryonic stem cell (hESC) derived insulin-producing cells are capable of functioning in rodents for over 200 days, suggesting this source of cells will provide the unlimited supply of cells necessary to create a cell product to treat insulin requiring diabetics.”

We wondered whether the HIP technology might prove more attractive than stem cell technology in deriving islets.

“As I mentioned above, this approach could obviate transplantation,” Musick said. “I feel that it is important to pursue both transplantation and regeneration from endogenous sources. Diabetes is a major global health care issue and all viable approaches to novel therapy need to be considered. Different approaches may also be more or less applicable to Type I or Type II diabetes.”

“Diabetes is a huge market opportunity,” Baird said, “and there are numerous approaches under investigation to treat both Type I and Type II diabetes. Enhancing beta cell mass to increase glucose related insulin levels is the ‘holy grail’ and has been elusive using both small molecule drugs and proteins/peptides to date.”

(Continued on page 7)
Musick did not see the CureDM technology as competitive, primarily because Vitro Bio-Pharma’s initial market for commercialization is “non-therapeutic applications in research, drug discovery and drug development.”

“I think that both therapeutic approaches need to be considered at this point,” he said. “It may well be that both transplantation and regeneration/modulation-elimination of autoimmune rejection will find a place in the clinic.”

Baird, however, was skeptical that the HIP technology would live up to its maker’s expectations.

“In the absence of peer reviewed data that has been confirmed by others, the approach can only be judged as marginal today,” she said. “Previous attempts at evaluating a similar protein in the clinic were unsuccessful. Also, demonstrating beneficial effects in vitro on beta cells has also been very difficult to replicate.”

She called it an “attractive approach” if a small molecule or protein therapy could actually restore beta cell function.

But, she added, HIP and related proteins have not convincingly demonstrated such effects. “Consequently, the only proven approach to achieving increased beta cell mass is to transplant islet cells directly into patients. In order to create sufficient insulin producing cells to treat the millions of patients who rely on exogenous insulin, hESC derived cells are the only cell therapy likely to provide a product capable of being manufactured and has already demonstrated efficacy in animal models of diabetes.”

CureDM, Inc., located at the Lankenau Institute for Medical Research on the Lankenau Hospital campus in Wynnewood, Pa., is developing peptide therapeutics using a platform that combines bioinformatics, proteomics and Human Genome sequence data.

This method has enabled the CureDM scientific team to determine the proteins involved in, and probable mechanisms of islet neogenesis in humans.

Contact: http://www.vitrodiag.com
Contact: http://www.novocell.com
Contact: http://www.curedm.com

Cytori Begins Breast Reconstruction Study In Europe

No Plans Yet For U.S. Studies

San Diego, Calif.-based Cytori Therapeutics (CYTX) said on May 1 that it has received approval to begin its European stem and regenerative cell-enhanced breast reconstruction study in breast cancer patients who have undergone partial mastectomy.

Enrollment was recently completed for a breast augmentation study in Japan, but a Cytori representative said the company does not yet have plans for similar studies in the United States. (See below.)

The new European study is a post-market study designated as RESTORE II.

Currently, there is no generally accepted reconstructive technique for partial mastectomy patients despite the fact that breast conserving therapy is standard practice in the treatment of women with breast cancer worldwide.

In this study, tissue loss resulting from partial mastectomy will be reconstructed with the patients’ own fat tissue (adipose), which will be enhanced with their adipose-derived stem and regenerative cells.

This procedure is referred to as cell-enhanced reconstruction.

The cells in RESTORE II will be made available at the time of surgery using Cytori’s Celution 800 System.

The primary goal is to obtain European reimbursement for cell-enhanced reconstruction using the Celution 800 System by measuring key quality of life improvements in breast cancer patients desiring reconstruction.

Up to 70 women will be enrolled at six clinical centers in the U.K., Italy, Spain, and France.

Primary endpoints will be patient and physician satisfaction with functional and cosmetic

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outcomes at six and 12 months after surgery. Cytori’s goal is to complete enrollment before the end of March 2009.

“RESTORE II is important for advancing reconstructive options for women with breast cancer,” said Prof. Emmanuel Delay, the study’s principal investigator and chief of plastic and reconstructive surgery at the Leon Berard Cancer Center in Lyon France. “A successful study should broaden availability of this therapy to partial mastectomy patients in Europe.”

“Unfortunately fewer options are available to women desperate for reconstructive surgery following partial mastectomy due to the effects of the adjuvant radiotherapy,” said Eva Weiler-Mithoff, surgeon at the Glasgow Royal Infirmary, and lead investigator for the U.K. study site. “Adipose tissue enriched with stem and regenerative cells represents a new approach that we believe allows for predictable graft retention.”

“My ongoing clinical experience using Cytori’s Celution 800 System in breast reconstruction has been very encouraging,” said Prof. Claudio Calabrese, associate professor of surgery and lead investigator at University of Florence Hospital. “The preliminary results warrant further investigation as part of the broader, post-market RESTORE II study.”

Secondary endpoints include six and 12-month assessments of breast volume and shape via magnetic resonance imaging (MRI) and improvement in skin pigmentation.

The study will evaluate patients who have undergone their last breast treatment at least 12-months prior and are recurrence free.

“The Celution 800 System is what makes this an effective, reproducible, bedside procedure,” said Cytori president Dr. Marc H. Hedrick. “Cytori has customized this system to provide a cell output specific to breast reconstruction, to be easy to use for doctors and hospitals, and to be affordable. We believe this mix of attributes combined with our goal of reimbursement could fill a tremendous patient and market need.”

Fat, known medically as adipose tissue, is the body’s richest known source of regenerative cells.

Adipose-derived regenerative cells include adult stem cells in addition to other important cell types that have been shown pre-clinically to improve tissue retention compared to non-cell-enhanced tissue transfers.

These results have been confirmed in physician-initiated clinical studies.

No Plans Yet For U.S. Studies

Cytori is now participating in breast reconstruction studies using adipose-derived stem cells in Japan and Europe.

Tom Baker, a spokesman for Cytori, told us that the company hopes to do more such studies in other parts of the world, but has “not yet laid out plans for U.S. clinical pathway/timing.”

Baker said other areas of the globe that are “definitely important” to the company include the Middle East and South America.

Competition From Other Stem Cell Sources

There’s been a lot of news lately about other sources of stem cells for use in research and therapy development.

These sources, which are being touted as alternatives to the use of human embryonic stem cells, include umbilical cord blood, placental tissue, menstrual blood, and induced pluripotent stem (iPS) cells derived from reprogrammed skin cells.

Cytori’s Baker, however, didn’t see these other alternatives as much of a threat to his company’s adipose-based stem cell technology.

“For reconstructive surgery, no other source presents a competitive threat because we're accessing cells from the source of the filler material,” he said. “This obviates the need for allogeneic cells or for getting cells from a source that's more difficult and invasive to access.”

But “for other indications,” he added, one source of stem cells might be “better suited for some diseases than others” and “no one source will completely dominate a particular therapeutic area.”

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The fact that there are so many different sources of stem cells, and the potential therapeutic markets are so large, means an advance in one sector is likely to have a positive impact on the other sectors, Baker said.

“The collective field will help each other advance and the markets are so large, there will be room for every source.”

“However,” Baker said, “there will be a distinct advantage to the source that gets to market first in each therapeutic area. This is our goal for each therapeutic area we’re pursuing.”

Cytori is dedicated to providing patients with new options for reconstructive surgery, developing treatments for cardiovascular disease, and banking patients’ adult stem and regenerative cells.

Contact: http://www.cytoritx.com

Company Announces Transplant Of Human Placenta-Derived Stem Cells

Summit, N.J.-based Celgene Cellular Therapeutics (CCT), a wholly owned subsidiary of Celgene Corporation (NASDAQ: CELG), on May 2 announced the clinical application of a human placenta-derived stem cells (HPDSCs) for hematopoietic reconstitution.

The groundbreaking transplant occurred at the LSU Health Sciences Center Children’s Hospital (LSU) on March 28, 2008, to treat a pediatric patient with acute lymphoblastic leukemia (ALL), a cancer of the bone marrow and blood.

Following the birth of the patient’s sibling in December 2007, HPDSCs, along with cord blood, were collected and cryo-preserved and both products were used in the transplant.

CCT owns proprietary technologies for collecting, processing, and storing HPDSCs.

HPDSCs are immature and versatile stem cells with potentially broad therapeutic applications in, for example, leukemia and other hematological malignancies, solid tumor cancers, and autoimmune diseases.

CCT is also conducting research on other types of stem cells derived from the placenta that are obtained via additional proprietary methodologies.

The transplant is part of a multicenter clinical trial being conducted at LSU, together with Morgan Stanley Children’s Hospital of New York-Presbyterian and Columbia University Medical Center using HPDSCs for patients with a range of disorders including cancers and non-malignancies.

It is a single-arm study with a primary objective of assessing the safety of transplantation of umbilical cord blood augmented with HPDSCs from the same donor, with a secondary objective of assessing potential restoration of normal hematopoiesis and immune function with this combination of cells.

Patients will be monitored carefully post-transplant for up to 24 months to monitor safety outcomes, engraftment, and survival.

“The patient is doing extremely well and, in fact, was discharged from the hospital one-to-two weeks earlier compared to traditional cord blood transplants,” said Lolie C. Yu, M.D., professor of pediatrics, division chief of the Pediatric Heme-Onc Program, director of the BMT Program at LSUHSC/Children’s Hospital.

“Neutrophil engraftment occurred earlier than anticipated in this proof-of-principle study further raising our hopes regarding the benefits of this treatment.”

There is considerable anticipation around the potential of HPDSCs.

An independent study headed by researchers from UCLA published earlier this year declared that blood-forming stem cells originate in the placenta in laboratory animals.

“We are excited to advance our study of the placenta as a source of stem cells that have the ability to effectively treat patients worldwide,” said CEO Robert Hariri, M.D., Ph.D. “We are pleased with this first positive step in our effort to

(Continued on page 10)
Graft vs. Host Disease (GVHD) occurs after a bone marrow transplant when the differences between a donor's marrow and recipient's tissues spark an immune response in the patient.

When the donor’s white blood cells recognize the recipient's body tissues as foreign, the transplanted bone marrow attacks the patient’s body.

The greater the mismatch between donor and recipient, the greater the risk of GVHD.

Drugs that suppress the immune system are usually given to patients following a marrow transplant to help prevent or reduce the severity of GVHD.

Current treatments are designed to suppress the patient’s immune response without damaging the new bone marrow.

Methotrexate and cyclosporine, either alone or in combination, are the medicines of choice.

Currently, the most effective treatment for acute GVHD is high-dose corticosteroids.

Patients who do not respond to steroids are given antibodies to T cells.

For chronic GVHD, patients are given the steroid prednisone alone or with the immune suppressant cyclosporin.

But what happens if these treatments fail to stop the disease?

In patients that fail to respond to steroids, mortality can reach 85 percent.

But that gloomy picture may be changing in the near future.

Columbia, Md.-based Osiris Therapeutics, Inc. (OSIR) has been developing a product it calls Prochymal to treat GVHD.

Prochymal is a formulation of adult mesenchymal stem cells obtained from the bone marrow of healthy adult donors and administered through a standard intravenous line.

Osiris is evaluating Prochymal in three, double-blind, placebo controlled Phase III studies, including steroid refractory GVHD, acute GVHD, and Crohn’s disease.

Prochymal has been granted fast track status by FDA for all three of these indications.

Prochymal also obtained orphan drug status by FDA and the European Medicines Agency for GVHD. FDA established the Fast Track program to accelerate the development of drugs that show promise for treating life-threatening conditions.

Orphan drug designation provides incentives to companies that develop drugs for underserved patient populations.

Prochymal is also being studied in a Phase II trial for the treatment of type 1 diabetes.

(Continued on page 11)
Objective clinical response to therapy, and 58 percent achieved complete resolution of their GVHD.

In a Phase II randomized, prospective trial evaluating Prochymal for acute GVHD in adults, 94 percent (29 of 31) responded after receiving two infusions of Prochymal, with 74 percent achieving complete resolution of their disease.

There were no infusional toxicities associated with the administration of Prochymal in either trial.

Under the expanded access program, children 2 months to 17 years in age inclusive with Grades B-D GVHD not responsive to steroids are eligible for treatment.

Osiris also markets and sells Osteocel for regenerating bone in orthopedic indications.

Osiris has also partnered with Genzyme Corporation to develop Prochymal as a medical countermeasure to nuclear terrorism and other radiological emergencies.

Prochymal is also being developed for the repair of heart tissue following a heart attack and for the protection of pancreatic islet cells in patients with type 1 diabetes.

The company’s pipeline of internally developed biologic drug candidates under evaluation also includes Chondrogen for arthritis in the knee.

(Continued on page 12)

Additionally, the Department of Defense recently awarded Osiris a $224.7 million contract to develop Prochymal for acute radiation syndrome.

**Expanded Access Treatment Program**

Now the company has announced it has been given clearance by the FDA to launch an expanded access treatment program for Prochymal, making the investigational stem cell product available to children with GVHD.

Congress and FDA created the expanded access program to facilitate the availability of promising new drugs to desperately ill patients before general marketing begins.

The program allows for investigational drugs to be made available to patients under certain circumstances during evaluation in late stage clinical trials when no satisfactory alternative therapy is available.

For expanded access, FDA must determine that the available scientific evidence, taken as a whole, demonstrates that the drug may be effective for its intended use or would not expose the patients to unreasonable and significant additional risk of illness or injury.

Additionally, FDA permits companies meeting certain criteria to charge for the investigational product.

“Prochymal has had a profound positive impact on the children that we have treated, all of whom had exhausted available therapeutic options,” said Paul Szabolcs, M.D., of the pediatric blood and marrow transplant program at Duke University. “Since there are no approved treatments for GVHD and mortality is so high, gaining faster and more reliable access to Prochymal will be very helpful to the families we serve.”

In support of the expanded access treatment program, Osiris submitted summary safety and efficacy data to FDA.

Prochymal was evaluated in pediatric patients suffering from severe GVHD that had failed, on average, three lines of therapy prior to entry into the trial.

All patients (12 of 12) experienced an objective clinical response to therapy, and 58 percent achieved complete resolution of their GVHD.

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**Bulletin: Osiris Jettisons Osteocel Business**

On May 8, it was announced that Osiris would be selling its Osteocel biologics business to NuVasive, Inc. (NUVA), a San Diego, Calif.-based medical device company that is developing products for minimally disruptive surgical treatments for the spine.

The Osteocel business includes a proprietary adult stem cell bone graft product containing beneficial properties similar to autograft, as well as a processing facility with significant supply stream capacity.

Selling the Osteocel product will bring in $85 million in cash and milestone payments, and will allow Osiris to focus its attention and resources on its stem cell product candidates.
Stem Cell Business News

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Osiris shares are traded on NASDAQ under the symbol OSIR.
Shares have traded in the range of $9.98 to $15.80 over the past 12 months.
Closing price as of May 8, 2008, was $11.77 per share.
Contact: http://www.Osiris.com

Braincells Launches Phase II Trial With Product For Depression With Anxiety

San Diego, Calif.-based BrainCells Inc. (BCI), said on April 17 that it has initiated a Phase IIa clinical trial with its lead product candidate for the treatment of depression with anxiety.

“We are encouraged by the enthusiasm expressed by our clinical investigators who view BCI-540 as a potential alternative to today’s widely prescribed treatments for depression,” said chief scientific officer Carrolee Barlow, M.D.

“Current therapies directly impact serotonin levels causing many unpleasant side effects, however we have shown that BCI-540 directly impacts neurogenesis without affecting serotonin levels. We are excited about the potential of this compound to change the way mood disorders are treated.”

The twelve-week randomized double-blind, placebo-controlled study will evaluate safety, efficacy and tolerability of BCI-540 to determine whether 80 mg given once or three times daily is effective in the treatment of depression with anxiety versus placebo.

“BCI is utilizing our understanding of the power of neurogenesis coupled with our proprietary neurogenic platform technology to identify a strong portfolio of clinical candidates, such as BCI-540, that we plan to move into the clinic this year,” said CEO Jim Schoeneck. “Moving BCI-540 into the clinic is an important milestone and we are now actively enrolling patients and anticipate completing enrollment by the end of this year.”

BrainCells is applying its proprietary neurogenesis platform technology to identify and reposition compounds for the treatment of central nervous system (CNS) diseases.

Neurogenesis is the process by which endogenous stem cells in the adult human brain produce new brain tissue, including neurons.

With its predictive screening platform, BCI can direct the selection and development of neurogenic compounds, increasing the opportunity for successful clinical trials in a variety of CNS indications.

Contact: http://www.braincellsinc.com

(Continued on page 13)

Finance & Funding

University of Edinburgh Human Embryonic Stem Cell Program Awarded UK Grants

The University of Edinburgh has received two grants totaling $7.2 million over two years from the UK Stem Cell Foundation, with funding from the Medical Research Council and Scottish Enterprise.

The grants relate to preclinical safety and efficacy studies of three therapeutic cell types derived from human embryonic stem cells (hESCs).

The projects are led by Dr. Brendon Noble and Prof. John Iredale at the University of Edinburgh’s MRC Centre for Regenerative Medicine.

The awards follow on from a collaboration set up in August 2006 between Menlo Park, Calif.-based Geron Corporation (GERN) and the University of Edinburgh to develop hESC-derived hepatocytes for the treatment of liver failure and for use in cell-based assays, as well as to develop osteoblasts and chondrocytes for the treatment of musculoskeletal disorders such as osteoporosis, bone fractures and osteoarthritis.

“These are the first grants we have awarded that use human embryonic stem cells,” said Sir Richard Sykes, chairman of the board of trustees, UK Stem Cell Foundation. “Our remit is to support high quality translational projects whose direct aim is rapid and safe progression towards clinical application. These research groups combine scientific and clinical expertise within a centre of excellence for stem cell research at the University of Edinburgh and are therefore well positioned for achieving success.”

(Continued on page 13)
“This funding and our continued collaboration with Geron will advance two important translational programs within the MRC Centre for Regenerative Medicine,” commented Prof. Sir John Savill, Head of College of Medicine and Veterinary Medicine at the University of Edinburgh. “The government has made a major investment in creating the Centre and this grant will allow us to progress toward our goal of delivering new treatments for debilitating diseases.”

Programs Funded by the Grant

Currently, the only treatment for chronic end-stage liver failure is whole organ liver transplantation, a costly procedure limited by the severe shortage of donor organs.

A potential alternative therapy being explored within the collaboration is the use of hepatocytes derived from hESCs either to restore liver function, or to be incorporated into bioartificial devices for patients awaiting transplantation or in need of short-term hepatic support.

In the liver program, recent improvements in the hepatocyte differentiation protocol have significantly increased the efficiency of producing functional human hepatocyte-like cells.

These derived cells have important genetic and functional characteristics of normal human hepatocytes, such as the expression of genes required for liver cell function and the ability of the cells to metabolize drugs.

The current funding will support preclinical studies to assess safety and efficacy of the hESC-derived hepatocyte-like cells.

An immediate goal of the work will be the development of the cells for drug testing.

Successful development of liver cells from hESCs will revolutionize and improve the way we are able to test drugs and novel therapies both for the liver and other organs in addition to the possible development of a stem-cell based approach to regenerate the liver.

Similarly, orthopedic indications are important targets for cell therapy, such as the replacement of degenerated cartilage in osteoarthritis, or of bone after trauma or osteoporosis, applications with major unmet needs.

These hESC-based therapies are intended to be off-the-shelf products, delivered on demand, and centrally produced from a uniform renewable source of undifferentiated cells, allowing efficient treatment of large numbers of patients.

The orthopedic program has derived bone forming osteoblasts and cartilage-forming chondrocytes from hESCs in vitro by directed differentiation and demonstrated survival of grafted cells in bone and cartilage repair sites in vivo.

Cells derived in this way have been shown to be capable of forming the authentic bone and cartilage material that is required to repair our skeleton and to be capable of doing this in sites in the body that need it.

The current funding will support further studies to assess safety and efficacy of hESC-derived osteoblasts and chondrocytes in preclinical models.

Bioactive scaffolds and cell carriers, developed at the University of Edinburgh, will be used to promote tissue regeneration in vivo.

Contact: http://www.scrm.ed.ac.uk
Contact: http://www.ukscf.org
Contact: http://www.geron.com

Aldagen Secures $18.4 Million in Financing

Durham, N.C.-based Aldagen, Inc. said on April 23 that it has raised $18.4 million in a private round of financing.

The financing was obtained from existing investors, including Intersouth Partners, Tullis-Dickerson, Herbert Venture Partners and The Aurora Funds.

The company plans to use the proceeds raised in this financing to further advance the development of its four clinical-stage product candidates and for general corporate purposes.

Aldagen is developing proprietary regenerative cell therapies that target significant unmet medical needs. The company has four product candidates in clinical trials.

Aldagen’s most advanced product candidate, ALD-101, is currently in a pivotal Phase III clinical trial to evaluate its effectiveness in improving cord blood transplants used to treat inherited metabolic diseases in pediatric patients.

The company also is conducting Phase I/II clinical trials on three product candidates: ALD 151 to improve cord blood transplants in the treatment of leukemias, ALD-301 to treat critical limb ischemia, and ALD-201 to treat ischemic heart failure.

Aldagen’s product candidates consist of specific populations of active adult stem cells that the company isolates using its proprietary technology.

Contact: http://www.aldagen.com

Briefly Noted

Bio-Matrix Applies For California Tissue Bank License

San Diego, Calif.-based Bio-Matrix Scientific Group Inc (BMSN), a biotechnology company focused on adult stem cell processing and cryogenic (Continued on page 14)
storage, said on May 5 that it has applied for a California tissue bank license.

The company said it had submitted required documentation including copies of its quality systems operating procedures to the California Health and Human Services Agency.

California requires human cell, tissue, cellular and tissue-based product facilities to follow the current Good Tissue Practice (GTP) standards, which govern the methods used in, and the facilities and controls used for, the manufacture and processing of human tissue, cellular and tissue-based products.

The company said a granting California tissue bank license would allow the it to process and store stem cells from adipose tissue (fat), cord blood and peripheral blood.

The company anticipates the banking of stem cells derived from adipose tissue (fat) has the potential to generate revenues of approximately $2,000 to $2,500 per specimen in first year fees followed by approximately $200 to $250 in annual maintenance fees per specimen per year.

The company also said it believes that, based on historical pricing trends, banking of umbilical cord blood specimens has the potential to generate revenues of $1,000 to $1,500 per specimen in first year fees followed by approximately $100 to $150 in annual maintenance fees per specimen per year.

Bio-Matrix hopes to become a leading source for stem cell research technology and innovation.

Contact: http://www.BMSN.us