Industry Update

Latest developments in stem cell research and regenerative medicine

Latest developments in the field of stem cell research and regenerative medicine compiled from publicly available information and press releases from nonacademic institutions from 1st January 2010 until 28th February 2010.

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Business Development

■ Collaborations, partnerships & alliances

Codevelopment agreement:

MedGenesis, Amgen & Biovail

MedGenesis Therapeutix Inc., BC, Canada (www.medgenesis.com), a biopharmaceutical company developing and commercializing innovative treatments for patients with serious CNS diseases, has entered into an agreement with Amgen Inc., CA, USA (www.amgen.com) granting MedGenesis an exclusive, worldwide license for glial cell line-derived neurotrophic factor (GDNF) protein in CNS and non-CNS indications, subject to the rights of a co-exclusive licensee for CNS indications in certain countries. GDNF is a naturally occurring growth factor capable of protecting and promoting the survival of dopamine-producing nerve cells. As part of the license agreement, Amgen now holds a small equity stake in MedGenesis. In parallel, Biovail Laboratories International SRL, a subsidiary of Biovail Corporation, MB, Canada (www.biovail.com), Canada's largest publicly traded pharmaceutical company, and MedGenesis have concluded an agreement to collaborate on the development of GDNF in Parkinson's disease, and potentially other CNS indications. Biovail, which is also a party to the Amgen license for CNS indications and has a co-exclusive license to exploit GDNF in certain countries (including the USA, Canada, Japan

and a number of European countries), contributes significant development expertise, a broad-based commercialization track record and a focus on CNS disorders. MedGenesis has also granted Biovail a license to its convection-enhanced delivery platform for use with GDNF in CNS indications. MedGenesis and Biovail will initially focus on the development of GDNF for Parkinson's disease, a progressive and debilitating neurological disease affecting close to 5 million patients worldwide.

Codevelopment agreement:

Roche, Massachusetts General Hospital & Harvard

Swiss-based giant Roche (www.roche.com) is teaming up with the Massachusetts General Hospital, MA, USA, and Harvard University, MA, USA (www.mgh.harvard.edu) to develop new stem cell-based cell lines as disease models for early drug candidate testing. The 3–5-year partnership will initially focus on metabolic disorders and cardiovascular disease and will expand to cover a range of other diseases. The collaboration aims to develop cell lines that can be used to evaluate the potential efficacy, safety and toxicology profiles of new drugs pulled from Roche's compound library. The company says that the cell lines will be derived from the tissues of both healthy volunteers and patients with a range of diseases. Roche will provide research funding over the term of the

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agreement and will have access to cell lines, protocols, data and materials. The firm will also pay clinical development milestones for drug candidates discovered through stem cell disease models. The ultimate goal is to use stem cells for discovering new treatment approaches and bridging the gap between the laboratory and the clinic. Roche has forged a number of collaborations focused on evaluating stem cell-based approaches for drug discovery. In June 2009, the firm signed a US\$10.36 million (~€7.5 million), 2-year collaboration with France-based Institute for Stem Cell Therapy and Exploration of Monogenic Diseases (I-STEM; www.istem.eu/ewb_pages/e/english.php) focused on the use of I-STEM's neuronal stem cell proliferation technologies in the screening of Roche's compounds for potential new candidates against neurodegenerative diseases. In 2008, Roche partnered with UK-based stem cell consortium Stem Cells 4 Safer Medicines (www.sc4sm.org) to generate a repository of stem cells suitable for toxicology testing in high-throughput platforms. The initiative is being funded primarily by the UK Government, with Roche and two other pharmaceutical companies also contributing. During the same year the firm signed an agreement with Cellular Dynamics, WI, USA (www.cellulardynamics.com) to test a number of its drug compounds for cardiotoxicity.

Codevelopment agreement:

Tissue Genesis & American Medical Systems Holdings

Tissue Genesis, Inc., HI, USA (www.tissuegenesis.com) and American Medical Systems Holdings, Inc., MI, USA (www.americanmedicalsistemas.com) have signed an agreement for the research and development of adipose-derived regenerative cells for use in treating pelvic health disorders. American Medical Systems will pay US\$1.1 million over the life of the agreement to obtain rights offered by Tissue Genesis, Inc. Through the deal, American Medical Systems has a 4-year option to obtain exclusive distribution and

license rights to Tissue Genesis' regenerative cell technology – including the Tissue Genesis Cell Isolation System™ – for use in human pelvic health applications, with an additional 2-year right of first refusal. Along with milestone payments, Tissue Genesis will receive rights to certain data and derivative technology developed under the agreement. Tissue Genesis, in turn, will provide American Medical Systems with instruments, disposables and know-how to allow American Medical Systems to develop state-of-the-art regenerative cell applications. The Tissue Genesis Cell Isolation System processes a small amount of the patient's own adipose tissue into a concentration of millions of regenerative cells, including adult stem cells, microvascular endothelial cells and other cells. These cells can be coated onto artificial implants or directly injected into damaged tissue, to improve circulation and support the formation of new tissue. The Cell Isolation System conveniently brings cell therapy solutions right to a patient's bedside, as it completes the process in approximately 1 h – in the operating room – while the surgeon prepares the patient to receive his or her own cells back into the damaged area. Through this new collaboration, American Medical Systems joins the Tissue Genesis Commercialization Consortium of companies, institutions and researchers who share their expertise. The consortium forms a network of top researchers in the field of adipose-derived regenerative cell technology for the mutual benefit of all the members.

Collaboration agreement:

Geron & the University of California

Geron Corporation, CA, USA (www.geron.com) has entered into a collaboration jointly funded by Geron and a University of California Discovery Research and Training Grant to investigate the therapeutic potential of its human embryonic stem cell (hESC)-based product, GRNOPC1, for Alzheimer's disease. The company is currently developing GRNOPC1 for the potential treatment of spinal cord injury. Under the collaboration, GRNOPC1 will be evaluated in models of Alzheimer's disease. The study is designed to assess whether memory,

which is impaired in the rodent models as it is in human patients, shows recovery after transplantation of GRNOPC1. The research will be led by Frank M LaFerla, Director of the Institute for Brain Aging and Dementia at the University of California, Irvine, CA, USA.

Distribution agreement:

Stematix & Laboratorios Bagó

Stematix, Inc. from TX, USA (www.stematix.com) entered into a 10-year exclusive agreement with Laboratorios Bagó (www.bago.com/BagoArg/Default.asp), a medical products company from Argentina. Under terms of the agreement, Laboratorios Bagó will distribute a variety of Stematix orthopedic and cellular products for use in regenerative and related medical treatments. The terms of the contract were not disclosed, but the contract also provides the option of additional forms of joint collaboration in clinical trials and treatments.

Distribution agreement:

ThermoGenesis & GE Healthcare

ThermoGenesis Corp. from CA, USA (www.thermogenesis.com) announced a new enhanced distribution agreement with GE Healthcare (www.gehealthcare.com), for its AXP® AutoXpress™ System used in the processing of cord blood. Under the revised distribution contract, which runs through July, 2012, GE Healthcare will continue to distribute the AXP product line, excluding certain countries in Latin and South America, Asia, the Commonwealth of Independent States and Eastern Europe. GE Healthcare will provide incremental funding for marketing support and market research beyond its previous commitments. The new arrangement also provides incentives for both parties related to sales success, product quality and delivery.

Marketing agreement:

BioTime & Millipore

BioTime, Inc., CA, USA (www.biotimeinc.com) shipped inventory of six ACTCellerate™ progenitor cell lines to its worldwide distributor, Millipore Corporation, MA, USA (www.millipore.com), according to the terms of the co-marketing agreement between the two companies announced in July 2009. Derived from

hESCs but not fully differentiated into specific cell types, each ACTCellerate™ line provides a convenient, highly purified source of progenitor cells that may have applications in drug discovery, research and the development of therapeutic products. BioTime's research products will soon be available to be ordered by researchers through Millipore's stem cell homepage, www.millipore.com/stemcells. Millipore, which is already a leading supplier of stem cell research reagents, plans a full launch for BioTime's progenitor cell lines and growth media during the first quarter of 2010.

Partnership agreement: **CORD:USE & Memorial** **Healthcare System**

In order to create a large, ethnically diverse, inventory of available cord blood stem cell units, CORD:USE Cord Blood Bank, FL, USA (www.corduse.com), is partnering with the Memorial Healthcare System (www.mhs.net), the fifth-largest public healthcare system in the nation, to collect umbilical cord blood that will be placed in a global registry for patients in need of a potentially life-saving transplant.

Service agreement:

Cord Blood America & BioCells

Cord Blood America, Inc., NV, USA (www.cordblood-america.com) has finalized an agreement to process and store cord blood specimens for BioCells, Inc. (www.biocells.com.ar/know.html), headquartered in Argentina, and its affiliates in Peru, Colombia, Bolivia, Panama and Puerto Rico. BioCells is the second largest stem cell storage company in Argentina with annual revenues of US\$1.5 million and 12 locations throughout that country, plus it recently expanded to both Uruguay and Paraguay.

Strategic alliance:

Roche & Singapore **biomedical technology**

Switzerland headquartered Roche (www.roche.com) is entering into a strategic alliance with Singapore's scientific and medical institutions to setup a major new translational research hub in Singapore. This 'Hub for Translational Medicine' aims to enhance the understanding of how scientific advances from preclinical research

can be transferred in practice to patients. Bringing together world-class expertise from Singapore's scientific and medical research institutions, with Roche's significant capability in translational medicine and clinical development, this new center will focus on expanding knowledge of disease biology to develop new personalized treatment approaches. With an investment of US\$93 million (100 million Swiss francs), the Hub for Translational Medicine will initially employ approximately 30 scientists. A joint steering committee, consisting of members from Roche and the Singapore institutes, will define the strategic direction of the alliance and oversee its research projects. Scientific and Medical Institutions involved include: Agency for Science, Technology and Research (A*STAR; www.a-star.edu.sg), The National University Hospital (www.nuh.com.sg), Nanyang Technological University (www.ntu.edu.sg), National Healthcare Group (www.nhg.com.sg) and Singapore Health Services Pte Ltd (www.singhealth.com.sg).

■ Launching new products **& services**

California Institute for **Regenerative Medicine**

The California Institute for Regenerative Medicine (CIRM; CA, USA) has launched an online stem cell curriculum for high school students. The home page for the portal is www.cirm.ca.gov/stem_cell_education_portal. The curriculum's first four units, which include modules on ESCs and adult stem cells, can be taught in a day or fill a school week, CIRM announced in a press release. The stem cell modules are designed for basic biology classes.

International Stem **Cell Corporation**

International Stem Cell Corporation from CA, USA (www.internationalstemcell.com) has signed up the first two *in vitro* fertilization clinics, California Center for Reproductive Medicine and Acacio Fertility Center, and engaged an experienced pharmaceutical industry executive to lead the establishment of the company's universal stem cell bank, UniStemCell™. The company uses unfertilized eggs (oocytes) to create human 'parthenogenic'

stem cells (hpSCs). Like ESCs, hpSCs are pluripotent, yet avoid ethical issues associated with the use or destruction of viable human embryos. Unlike induced pluripotent stem cells (iPSCs), hpSCs do not involve extensive gene manipulation, which may have unknown biological impact. Unlike both ESCs and iPSCs, hpSCs can be created in a homozygous form such that each line will be an immunological match for millions of patients.

Natasha's Place

Natasha's Place (www.natashasplace.org), is the first cord-blood bank in USA with an emphasis on mixed heritage and minorities. The organization will reach out to African-Americans, Asians, Latinos and other minorities. Natasha's Place uses ethnodemographics and DNA identification to establish matches. All the public cord blood information will go into a global registry.

Novartis & BloodSource

Since its founding in 1948, BloodSource has been collecting blood donations and providing life-saving blood products to California communities and beyond. They are currently completely covering nearly 40 hospitals in 25 Californian counties. However, only one in five African-Americans who need a life-saving bone marrow transplant will receive one because not enough African-Americans donate blood and bone marrow. BloodSource and Novartis Diagnostics announced a partnership to change that. The Sacramento-based blood bank and Emeryville division of the Swiss firm Novartis are kicking off an advertising and community outreach program to encourage African-Americans to donate blood and register as bone-marrow donors. The campaign is funded by a grant from Novartis, Basel, Switzerland, but the company declined to comment on the amount.

StemCyte

StemCyte Inc., from CA, USA (www.stemcyteinc.com), will be opening its first umbilical cord-blood stem cell banking

facility at Apollo Hospital in Gujarat's Gandhinagar district. It will be the first cord-blood bank facility in India that will be used for both public and family donor purposes. The stem cell bank is a tripartite venture between StemCyt India Therapeutics, Apollo (www.apollo-hospitals.com) and Indravadan Modi-led Cadila Pharma (www.cadilapharma.com), Ahmedabad, India. The company plans to build an inventory of 25,000 ethnically diverse units here to help treat critically ill patients in India and abroad, and also facilitate stem cell transplantation through Apollo Hospitals.

■ Advancements

Advanced Cell Technology

Advanced Cell Technology, MA, USA (www.advancedcell.com) demonstrated that human iPSCs are capable of generating hemangioblasts/blast cells (BCs), endothelial cells and hematopoietic cells with phenotypic and morphological characteristics similar to those derived from hESCs, but with a dramatic decreased efficiency [1]. Furthermore, in distinct contrast to the hESC derivatives, functional differences were observed in BCs derived from human iPSCs, including significantly increased

apoptosis, severely limited growth and expansion capability, as well as a substantially decreased hematopoietic colony forming capability. After further differentiation into erythroid cells, a greater than 1000-fold difference in expansion capability was observed in human iPSC-BCs versus hESC-BCs. Although endothelial cells derived from human iPSCs were capable of taking up acetylated low-density lipoprotein and forming capillary-vascular-like structures on Matrigel™ (BD Biosciences, CA, USA), these cells also demonstrated early cellular senescence. Similarly, retinal pigmented epithelium cells derived from human iPSCs began senescing in the first passage. Before clinical application, it will be necessary to determine the cause and extent of such abnormalities, and whether they also occur in human iPSCs generated using different reprogramming methods.

ReNeuron

British biotech company ReNeuron, Guildford, UK (www.reneuron.com) announced that its ongoing US collaboration with the Schepens Eye Research Institute at Harvard Medical School (MA, USA) will benefit from an unrestricted grant to advance retinal research at Schepens from a leading US speciality healthcare company. This funding will be directed towards the first phase of a 2-year translational program to take human

retinal progenitor cells (hRPCs) towards the clinic in the US, initially as a candidate cell-based therapy for retinitis pigmentosa, a disease of the retina that causes blindness. ReNeuron has designated this first retinal candidate as ReN003. The first phase of the program will involve studies to demonstrate a functional improvement of vision after grafting of hRPCs in ophthalmic disease models. Systemic approaches to optimize the yield of hRPCs in culture will also be carried out in this next phase of the collaboration, ahead of future GMP manufacture of the cells. Last year, researchers at the Schepens published two reports describing the growth kinetics and molecular characterization of hRPCs developed under the collaboration with ReNeuron and their ability to differentiate along the photoreceptor lineage, both *in vitro* and *in vivo* [2,3]. Following transplantation in a rodent model of damaged retina, the hRPCs were seen to integrate with the host retinal tissue and differentiate to express the protein rhodopsin, a marker for the light-sensitive rod cells found in healthy retina. Importantly, although retinitis pigmentosa is the initial target disease in ReNeuron's collaboration with Schepens, the hRPCs developed in the program will almost certainly be applicable as cell therapy candidates for other blindness-causing diseases, such as age-related macular degeneration and diabetic retinopathy.

Clinical Trials

■ Aastrom

Aastrom Biosciences, Inc., from MI, USA (www.aastrom.com), reported results from a planned interim analysis of the company's multicenter, randomized double-blind placebo-controlled US Phase IIb clinical trial designated RESTORE-CLI. According to the interim analysis, the safety profile was similar between the treatment and placebo arms. Based on a composite efficacy end point assessing time to treatment failure (including major amputations, wound size and gangrene), Aastrom's autologous

vascular repair cells were more effective than placebo ($p < 0.05$). Other clinically meaningful end points (e.g., major amputation rate and complete wound closure) approached but did not reach statistical significance at interim analysis. A total of 46 critical limb ischemia patients who had at least 6-month follow-up, including 33 patients with 12-month follow-up, contributed to the interim analysis. Further information regarding this clinical trial is available on www.clinicaltrials.gov (ID: NCT00468000).

■ Bioheart

Bioheart, Inc., FL, USA (www.bioheartinc.com), has commenced work on its REGEN trial, a Phase I clinical trial to test genetically modified MyoCell® in patients suffering from congestive heart failure. Bioheart's MyoCell is a regenerative cell therapy that uses myoblasts grown from a patient's own muscle. MyoCell has been tested successfully on patients in four clinical trials. The REGEN trial is designed to test the safety and effectiveness of a composition of muscle stem cells that have been gene modified

to induce a greater-than-usual release of the stromal cell-derived factor (SDF)-1 protein. The SDF-1 protein is a molecule in the human body that, after an injury, is naturally released by most tissues to attract stem cells. Unlike other tissues, the heart muscle does not release enough SDF-1 to attract the number of stem cells that would result in complete self-healing. As a result, scar tissue forms and impairs normal heart function. Results from Bioheart's preclinical animal studies have shown that the genetically modified MyoCell is far more effective than MyoCell alone in accomplishing repair and tissue regeneration. With SDF-1, there is a release of additional therapeutic proteins to assist in the tissue repair process, resulting in a more expansive and quicker repair. The REGEN trial is being funded by one of the company's institutional investors, the Ascent Medical Technology Funds, and the Philadelphia BioMed Product Development Centre, PSC, a preclinical and clinical research organization, is responsible for the study. The trial is being conducted in Jordan whose clinical research capabilities and facilities rival those in the USA and Europe. The country's leadership in medicine has made it a destination for patients from the Middle East, Europe, south Asia and even the USA for treatments that encompass the full range of complexity, including the most innovative procedures for ameliorating cardiovascular disease and cancers. The Jordanian government and medical community have commenced programs on cell and stem cell therapies, establishing four research centers to concentrate on these disorders.

■ Cord Blood Registry

The Medical College of Georgia is conducting the first US FDA-approved clinical trial to determine whether an infusion

of stem cells from umbilical cord blood can improve the quality of life for children with cerebral palsy. The study will include 40 children, aged 2–12 years, whose parents have stored cord blood at the Cord Blood Registry from AZ, USA (www.cordblood.com). Further information regarding this clinical trial is available on www.clinicaltrials.gov (ID: NCT 01072370).

■ ReNeuron

British biotech company, ReNeuron and a team of doctors in Scotland have won final approval to start a pioneering clinical trial to assess whether stem cell therapy can help patients disabled by stroke. The treatment involves injecting neural stem cells developed from human fetuses into patients' brains in the hope they will repair areas damaged by stroke, thereby improving both mental and physical function. The final green light from Britain's Gene Therapy Advisory Committee (GTAC), announced on Wednesday, follows months of delays and questions, reflecting the ground-breaking nature of the research. ReNeuron received approval from Britain's main drugs watchdog back in January 2009 but still needed a recommendation from the GTAC before it could start the Phase I clinical trial. The first patient in the study is now expected to receive treatment through the National Health Service at the Institute of Neurological Sciences, Southern General Hospital, Glasgow, during the second quarter of this year. In total, 12 patients will get ReNeuron's ReN001 cell therapy between 6 and 24 months after having an ischemic stroke – caused by a blockage of blood flow in the brain – and their progress will be followed for 2 years. The procedure involves the direct injection

of millions of cells into the affected brain region. The initial tests will look primarily at the safety and feasibility of the treatment. If the first study is successful, researchers plan to pursue accelerated clinical development in later-stage clinical trials, focusing initially on more severely disabled stroke patients.

■ StemCells

StemCells, Inc. from CA, USA (www.stemcellsinc.com) announced that its proprietary HuCNS-SC® human neural stem cells have been used to treat the first patient enrolled in its Phase I clinical trial in Pelizaeus–Merzbacher disease (PMD), a myelination disorder that afflicts male children. The stem cells were administered at the University of California (www.ucsf.edu) Children's Hospital (San Francisco, CA, USA) by direct injection into the brain of a patient with congenital PMD, the most severe form of the disease. This marks the first time that neural stem cells have been transplanted as a potential treatment for a myelination disorder, and the second clinical trial involving the use of HuCNS-SC cells in a neurodegenerative disease. Patients with PMD are born with a defective gene leading to insufficient myelin in the brain. Those with the most severe form of the disease, congenital PMD, lose the ability to walk and talk, and eventually die, often before the age of 10 years. Currently, there are no effective treatments for PMD. Further information regarding this clinical trial is available on www.clinicaltrials.gov (ID: NCT 01005004).

Regulations, approvals & acquisitions

■ Green light

Cytori

The FDA has granted Cytori Therapeutics, CA, USA (www.cytori.com) 510(k) marketing clearance for its PureGraft™

system. Cytori will now launch the first and only device in the USA cleared for esthetic body contouring using autologous fat. PureGraft allows a patient's own fat tissue to rapidly be prepared in approximately

15 min for reinjection back into the same patient for aesthetic contouring. PureGraft is able to prepare both small and large volumes of fat grafting tissue ranging from 50 to 250 ml. PureGraft maintains sterility

while optimizing the yield of tissue to be grafted, which provides significant utility to physicians. In contrast to traditional methods of graft preparation, PureGraft washes the graft and drains the tumescent fluid, free lipid and debris in a closed sterile system, allowing for a cleaner graft in less time than it would take to prepare a comparable volume of graft tissue traditionally.

Mesynthes

Mesynthes, a privately held regenerative medicine company from New Zealand (www.mesynthes.com), announced that the FDA has granted 510(k) clearance for the company's Endoform Dermal Template™. Endoform, a proprietary extracellular matrix biomaterial, provides a unique biologic template for tissue regeneration. Endoform technology utilizes a proprietary extracellular matrix biomaterial containing a complex mixture of important biological molecules, including structural and adhesive proteins such as collagens, elastin, fibronectin and laminin, and glycosaminoglycans. Endoform Dermal Template is presented as a sterile dry sheet in a peel pouch and is strong and easy to handle in a dry or wet state. It is applied directly to the wound bed, then rehydrated, covered with a nonadherent dressing and secured in place. Endoform is quick and easy to apply, available off the shelf and does not require special storage. It is intended for the management of a wide variety of wounds including: partial and full-thickness wounds, pressure ulcers, venous ulcers, diabetic ulcers, chronic vascular ulcers, tunneled/undermined wounds, surgical wounds (donor sites/grafts, post-Moh's surgery, postlaser surgery, podiatric and wound dehiscence), trauma wounds (abrasions, lacerations, second-degree burns and skin tears) and draining wounds.

TCA Cellular Therapy

The FDA (www.fda.gov) gave a green light to TCA Cellular Therapy, LLC, LA, USA (www.tcacellularthrapy.com) to conduct Phase I clinical trials for the treatment of amyotrophic lateral sclerosis

(ALS or Lou Gehrig's disease) using proprietary adult stem cell protocol. This is the second FDA-approved protocol for the treatment of ALS using stem cells in the USA; and the first using adult stem cells from the same patient. The aim of the Phase I study will assess safety. The procedure from the vantage point of the patient is rather simple. Bone marrow is removed from the rear hip through a minimally invasive, in-office procedure. The cells are then separated into the endothelial progenitor and mesenchymal stem cells. The cells are then washed and placed in a special medium for expansion. Over a 2–3-week period, the original 1000 cells grow into 30–40 million cells while in a specialized incubator. Once they have multiplied, the cells go through a seven-step protocol to check the cells prior to patient infusion, which is similar to a blood transfusion or injection.

■ Approvals

Lifebank

Lifebank Corp., BC, Canada (www.lifebank.com) has become the first and only cord-blood bank in Canada to earn the industry's highest accreditation from the Foundation of Accreditation of Cellular Therapy ('FACT'). FACT accreditation is considered the gold standard of quality, performance and integrity by a defined group of leading experts in the field of cord-blood banking. Lifebank is now fully FACT-accredited by demonstrating compliance with the NETCORD-FACT International Standards for Cord Blood Collection, Processing, Testing, Banking, Selection and Release.

■ Acquisitions

Allergan & Serica

Serica Technologies Inc., MA, USA (www.sericainc.com) has been acquired by Allergan Inc., CA, USA (www.allergan.com). Under terms of the deal, Serica is operating as a wholly owned subsidiary of Allergan and will continue working out of its R&D and manufacturing facility in Medford, MA, USA. Serica stockholders pulled in a cash payment and equity in another firm, Alacer Biomedical Inc., which holds exclusive rights to Serica's intellectual property, as related to orthopedic and veterinary applications. Neither

company revealed the financial terms of the acquisition. Serica raised approximately US\$14.5 million in venture capital fundraising from Prism VentureWorks, Morningside Technology Ventures and Ivy Capital Partners. Serica develops silk-based biomaterials used to repair tissue and ligaments. Formerly named Tissue Regeneration Inc., the company was founded in 1998 by Gregory Altman. Altman, CEO of the company, developed the firm's technology after he ruptured his anterior cruciate ligament while playing varsity football at Tufts University. In February 2009, Serica was granted FDA 510(k) clearance for its SeriScaffold soft tissue repair technology.

■ Patents

Fate Therapeutics

Fate Therapeutics, Inc., from CA, USA (www.fatetherapeutics.com) received a Notice of Allowance from the US Patent and Trademark Office (www.uspto.gov) for US Patent Application Number 10/997,146 entitled 'Methods for Reprogramming Somatic Cells'. Upon issuance, the patent will cover foundational iPSC technology for identifying agents that enable the reprogramming of human somatic cells, including pluripotency genes, small molecules and biologics. The invention by Rudolf Jaenisch, founding member of the Whitehead Institute for Biomedical Research and scientific founder of Fate Therapeutics, has a priority date of 26 November 2003 and is believed to be the earliest art that describes broad methods and key agents to reprogram human somatic cells to a pluripotent state. Fate Therapeutics holds an exclusive license to the application in commercial fields, including for drug discovery and therapeutic purposes.

iPierian

Induced pluripotent stem cell company iPierian from CA, USA (www.ipierian.com) has received from the Intellectual Property Office in the UK a Notification of Grant for the patent number GB2450603. The patent covers the generation of human iPSCs from human postnatal cells through any combination of forced expression of genes, which include the *Oct3/4*, *Sox2* and *KFL4*

genes, so long as the combination does not include a potentially cancer causing gene *c-Myc*. This is the first patent protecting a fundamental method and utility of human iPSC technology that has been granted outside of Japan.

■ Capital market & finances

BioTime/OncoCyte

BioTime, Inc., CA, USA (www.biotimeinc.com) announced that its subsidiary OncoCyte Corporation has completed the funding of the second tranche of a private equity offering through the sale of 3 million shares of OncoCyte common stock for US\$2 million to a private investor. BioTime plans to invest an additional \$2 million of its own cash in OncoCyte during the first quarter of 2010. OncoCyte plans to use these funds to accelerate its research efforts and to further develop its management team, staff and business. OncoCyte's therapeutic strategy and goal is to utilize hESC technology to create genetically modified stem cells capable of homing to specific malignant tumors while carrying genes that can cause the destruction of the cancer cells. This therapeutic use of hESCs differs from most proposed industrial uses of stem cell technology, in that OncoCyte's goal is not the stable engraftment of the cells to regenerate tissue function, but rather a use of the unique properties of stem cells as a tool to eliminate malignant cells. OncoCyte believes that its unique therapeutic strategy may be well-suited to the treatment of certain cancers for which no current therapies are effective; therefore, fulfilling a current high unmet medical need.

BrainStorm

BrainStorm Cell Therapeutics Inc., Israeli (www.brainstorm-cell.com) has entered into agreements with three investors, each investing US\$500,000 for a total of investment of \$1.5 million into BrainStorm. The agreements require the company to issue, to each of the three investors, 2 million shares of the company's stock based on the 30-day average share price as of 11 February 2010 of \$0.25 per share, and 1 million warrants with an exercise price of \$0.50 per share for a total issuance of 6 million shares and 3 million warrants. Along with these investors, ACCBT Corporation will invest its

remaining commitment of approximately \$500,000 in the company. Together, these investments provide BrainStorm with the necessary funds to conduct its upcoming Phase I/II ALS clinical trials.

Cellular Dynamics International

Cellular Dynamics International from WI, USA (www.cellulardynamics.com) has raised US\$40.6 million, according to a filing the company made with the Securities and Exchange Commission. The Securities and Exchange Commission filing does not disclose the names of the investors involved and does not detail the structure of the offering. The company previously raised \$18 million in late 2008 from mostly Wisconsin-based investors.

China Cord Blood Corporation

China Cord Blood Corporation, Hong Kong (www.chinacordbloodcorp.com), the first and the largest cord-blood banking operator in China, in terms of geographical coverage, and the only cord-blood bank operator with more than one license (i.e., Beijing and Guangdong), has exercised the remaining portion of their over-allotment option, bringing the total gross proceeds of the public offering to US\$23 million. China Cord Blood Corporation intends to use the net proceeds from the offering for the expansion into new geographical markets, including applications for new licenses and acquisitions and investments, and for the construction and upgrading of facilities in existing geographical markets.

Cord Blood America

Cord Blood America, Inc., NV, USA (www.cordblood-america.com) has completed capital raises over the last 18 months totaling US\$16.8 million, including a new \$3 million financing focused on avoiding dilution and being investor-friendly as Cord Blood America puts in place its business strategy for success in 2010. Specifically, Cord Blood America raised \$4 million in a short-term equity line in July 2008, \$2.3 million in convertible debt in April 2009, \$7.5 million in long-term equity in June 2009 and entered into agreements for \$3 million in January 2010 targeted specifically for acquisitions.

Living Cell Technologies & CytoSolv

Australia- and New Zealand-based Living Cell Technologies Ltd. (www.lctglobal.com) has received 10% ownership of USA-based CytoSolv Inc. (www.cytosolv.com), in exchange for restricted supply of choroid plexus cell clusters from its designated pathogen free pig herd and granting CytoSolv a nonexclusive, nontransferable license to use its broad choroid plexus patents solely for the purpose of wound healing. CytoSolv is a biomedical company developing proprietary technology to address wound healing, initially targeting diabetic ulcers. Its technology involves the delivery of a mixture of wound healing factors derived from porcine choroid plexus cells cultured using proprietary techniques. These cells normally secrete a variety of factors into the cerebrospinal fluid that are responsible for growth, differentiation, nurturing and maintenance of the brain. CytoSolv has demonstrated that a topical gel based on a cocktail of these factors accelerates and improves the quality of healing of open skin wounds, and has recently been awarded US\$500,000 from the Slater Technology Fund to pursue more advanced preclinical development in the year ahead.

Neuralstem

Neuralstem, Inc., MD, USA (www.neuralstem.com) has raised a total of US\$5,228,000 since the beginning of the year until 18 February 2010, comprised of a previously disclosed \$1.5 million private placement of 646,551 common shares at \$2.32, priced at a 30% premium over the market on the closing, and approximately \$3.7 million from warrant exercises. Consequently, Neuralstem received notice from the New York Stock Exchange Amex that the company is now in compliance with its listing requirements.

Shenzhen Beike Biotechnology

The Jiangsu Government's Science and Technology Department has announced a US\$1.8 million grant – the

Jiangsu Technological Achievements Transformational Grant – to support the research and development of human umbilical cord mesenchymal stem cell (hUC-MSC) technologies. The grant recipient and administrator, Shenzhen Beike Biotechnology Co., Ltd. (www.beikebiotech.com), is working with Jiangsu University and Nanjing University's Drum Tower Hospital to fulfill the grant's requirements. This grant marks the start of the second stage of Beike's stem cell engineering industrialization project. The project's first phase began in May 2008, when Beike opened a 1800 m² stem cell bank in Taizhou's China Medical City district. In the second phase, the bank will be used as a library for storing and indexing hUC-MSC samples. In April 2009, Beike broke ground on its 20,000 m² Stem Cell Regenerative Medicine Industrial Complex, the world's largest stem cell

storage and processing facility. Beike will use a portion of the Jiangsu Technological Achievements Transformational Grant to outfit this complex with over 80 specialized pieces of equipment, including fully automated enzyme immunoassay analysis systems, carbon dioxide incubators and cell viability analyzers. The grant's 3-year objectives are to systematically develop hUC-MSC technology and its medical application from 'bench-to-bedside' – from harvesting, to laboratory modeling, through clinical trials and finally clinical applications in treating systemic lupus erythematosus, multiple sclerosis and other degenerative diseases. In support of this effort, Beike will provide the facilities, equipment, management framework and certain proprietary clinical stem cell technologies for the project. Nanjing University Medical School's Drum Tower Hospital will be responsible for administering the human trials while Jiangsu University will be responsible for the production and animal study phases of the project. Both institutions are from Jiangsu province in China.

Financial & competing interests disclosure

The author has no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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