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 1 May 2013 until 30 June 2013.

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Business Development

■ Collaborations, partnerships & alliances

Codevelopment agreement: NGM Biopharmaceuticals & MedImmune
NGM Biopharmaceuticals, CA, USA (www.ngmbio.com), and MedImmune, CA, USA (www.medimmune.com), the global biologics research and development arm of AstraZeneca, UK (www.astrazeneca.com), have entered into an exclusive agreement to discover, develop and commercialize novel therapeutics from NGM's enteroendocrine cell program for the treatment of Type 2 diabetes and obesity.

Collaboration agreement: Epistem & ScandiDerma

Epistem, UK (www.epistem.co.uk), and ScandiDerma, Norway (www.scandiderma.com), aim to develop together a new *in vitro* human living skin-equivalent model for testing inflammatory responses. Epistem's expertise is in the regulation of adult stem cells in epithelial tissue, which includes the skin, hair follicles, GI tract, breast and prostate. ScandiDerma is focused on developing new dermatological products from biomass. The collaboration is made possible through the UK's innovation agency, the Technology Strategy Board (www.innovateuk.org), and Innovation Norway (<http://innovasjonnorge.no>), following a successful application for funding in the 'Sustainable high value chemical manufacture through industrial biotechnology' competition.

Distribution agreement: Stemedica Cell Technologies & Life Technologies

Stemedica Cell Technologies, CA, USA (www.stemedica.com), have entered into a global distribution agreement with Life Technologies, CA, USA (www.lifetech.com). Under the terms of this agreement, Life Technologies will exclusively offer Stemedica's ischemic tolerant allogeneic adult mesenchymal stem cells and neural stem cells for sale worldwide. Stemedica stem cell lines will be sold under the brand name Gibco® and are available to purchase for research initiatives beginning of the second quarter of 2013. The label will also carry the name of Stemedica as the manufacturer of the cell lines.

Partnership agreement: Cell Therapy Catapult & GlaxoSmithKline

The Cell Therapy Catapult, UK (<http://ct.catapult.org.uk>), which is focused on the development of the UK cell therapy industry to increase the nation's health and wealth, will be working with GlaxoSmithKline, UK (www.gsk.com), to explore potential collaborations in a range of areas relevant to the development of cell therapies, from research projects to technical and regulatory strategy.

Partnership agreement: Pluristem Therapeutics & Cha Bio & Diostech
Pluristem Therapeutics, Israel (www.pluristem.com), has entered into an

exclusive out-license and strategic partnership agreement with Cha Bio & Diotech, South Korea (<http://en.chabio.com>), for the use of Pluristem's PLacental eXpanded (PLX) cells for peripheral artery disease, specifically in two indications in South Korea: the treatment of critical limb ischemia and intermediate claudication. Under the terms of the agreement, Cha will perform and fund multiple clinical trials in South Korea under the supervision of The Ministry of Food and Drug Safety (MFDS), formerly known as the Korea Food & Drug Administration (KFDA). Upon the first regulatory approval for a PLX product in South Korea, Pluristem and Cha will establish a joint venture co-owned by the parties.

■ Launching new projects, products & services

AMSBio

AMSBio, UK (www.amsbio.com), has introduced a new range of 96-well format 3D Spheroid Cell Proliferation/Viability Assays, providing a new tool to allow cell-based assays to be carried out in 3D. The assay offers an *in vitro*, standardized, 3D, high-content format for inducing multicellular tumor spheroid formation and quantitating cell viability within the spheroids in response to pharmacological treatment. Physiological gradients for nutrients, oxygen, catabolites and pH due to limitations in diffusion through multicellular layers promote the creation of heterogeneous cell populations with proliferating cells on the spheroid surface, quiescent cells in the intermediate layers and necrotic cells in the core, similar to an avascular tumor. Uniform spheroid size and physiology is determined through cell seeding, providing a robust and reproducible assay format for drug screening or pathway analysis.

Arteriocyte

Arteriocyte, OH, USA (www.arteriocyte.com), launched Compass Biomedical, OH, USA (www.compassbiomed.com), the commercial tools division that supplies novel cell culturing products and

technologies for translational research. Compass Biomedical already supplies three product lines: NANEX™ Cell Culture and Expansion Kit; Adhere-34™ Cell Culture and Expansion Bag; and PLUS™ Cell Culture Supplement.

Cellular Dynamics International

Cellular Dynamics International, WI, USA (www.cellulardynamics.com), now offers through its MyCell® product line access to a number of disease models, including cardiomyopathies and arrhythmias, vision disorders, neurological disorders and muscular dystrophies. In addition, the company is actively working on expanding its disease model offering, currently working on additional disease models for neurodegenerative disorders and drug-induced liver injury. In addition, the company has licensed Life Technologies', CA, USA (www.lifetech.com), GeneArt® Precision TALs (TALENs) and Sigma-Aldrich's, MO, USA (www.sigmaaldrich.com/sigma-aldrich/home.html), CompoZr® Zinc Finger Nuclease Technology, enabling targeted gene insertions, deletions or modifications specified by the customer.

Cell Therapy Catapult

The Cell Therapy Catapult (<http://ct.catapult.org.uk>), has published its database of ongoing preclinical research in this area in the UK. It details 37 cell therapy projects, which it believes to be 2 years or less from the clinic, and will be used by the Catapult to track cell therapy trends and to guide its future activities.

CiRA

Kyoto University's Center for iPSC Research and Application, Japan (CiRA; www.cira.kyoto-u.ac.jp/e), has started to provide eight disease-specific patient-derived iPSC lines through RIKEN Bio-Resource center (www.brc.riken.jp/inf/en/index.shtml): three lines of chronic infantile neurological cutaneous and articular syndrome and five lines of amyotrophic lateral sclerosis. These cell lines are available for nonprofit organizations for the purpose of academic research. Some of them, however, are available for profit-making organizations under some conditions. When new lines of disease-specific

iPSCs become available, it will be notified on the CiRA website.

CordBlood America

Cord Blood America, NV, USA (www.cordblood-america.com), launched a new service CordMatrix™ offering for the storage of mesenchymal stem cell from umbilical cord as both a stand-alone service and in combination with the umbilical cord blood, through its wholly owned subsidiary CorCell Companies, NV, USA (www.corcell.com).

EMD Millipore & Plasticell

EMD Millipore (www.emdmillipore.com), the Life Science division of Merck, Germany (www.merck.com), and Plasticell, UK (www.plasticell.co.uk), announced the availability of OsteoMAX-XF™, the first fully defined, xeno-free medium for the differentiation of human mesenchymal stem cells into osteocytes. Mineralization can be detected in less than 1 week. The optimized, single-application osteogenic medium was developed using Plasticell's combinatorial screening system that performed a rapid screen of 3375 combinations of fully defined cell culture media, equivalent to hundreds of thousands of combinations of media components.

Genetics Policy Institute

Genetics Policy Institute, FL, USA (GPI; www.genpol.org), opened a new office in Washington, DC, USA. This new location will also give GPI the opportunity to begin hosting an array of high-level workshops, seminars and events aimed at removing roadblocks to innovative biomedical solutions found within the fields of stem cell research and regenerative medicine.

Life Technologies

Life Technologies, CA, USA (www.lifetech.com), launched the TaqMan® hPSC Scorecard™ Panel, a first-of-its-kind characterization assay that establishes a standardized benchmark against which researchers can now evaluate pluripotency and three lineage differentiation potential in human embryonic stem cell and induced pluripotent stem cell lines. The company also launched Epi5™ Episomal iPSC Reprogramming Vectors.

Nanofiber Solutions

Nanofiber Solutions, OH, USA (www.nanofibersolutions.com), launched NanoHep, a new cell culture system specifically for hepatocyte culture. NanoHep is made of specially treated electrospun nylon nanofibers that provide a 3D *in vivo*-like matrix for superior cell attachment and greater CYP450 enzyme expression, specifically CYP1A2, CYP2B6 and CYP3A4. NanoHep allows live-cell imaging and is compatible with standard downstream applications and high-throughput automated assays.

National Institute of Standards & Technology

The National Institute of Standards and Technology, MD, USA (NIST; www.nist.gov), has issued a new reference material – a sort of standardized sample – of cellular scaffolds for use in tissue engineering research [101]. Each unit of NIST Reference Material 8394, ‘tissue engineering reference scaffolds for cell culture’, includes 24 ‘free-form’ scaffolds made of poly- β -caprolactone in a standard 96-well plate. Each scaffold has six layers of poly- β -caprolactone struts laid down in a crisscross pattern. NIST provides reference values for the diameter, spacing and porosity of the struts, as well as adhesion and proliferation of osteoblasts.

RepliCel

RepliCel Life Sciences, BC, Canada (www.replicel.com), initiated the clinical development of a new autologous cell therapy for the treatment of a variety of chronic tendon injuries. Preclinical research, as well as published clinical Phase I data, indicates that the engraftment of collagen-producing fibroblasts from the dermal sheath of a hair follicle can repair microtears and promote the regeneration of damaged tendons associated with chronic tendinosis. Phase I work in humans, using fibroblast cells derived from adipose tissue, produced statistically significant improvements in function and pain. RepliCel is planning a Phase II

Achilles tendinosis trial using a new source of cells, fibroblasts isolated from nonbulbar dermal sheath cells of a hair follicle. This tendon technology, named RepliCel Tendon-01 (RCT-01), will be tested in approximately 90–120 subjects in a Phase II trial anticipated to commence in late 2013. RepliCel’s focus on the use of nonbulbar dermal sheath cells is based on the fact that these cells produce significantly more type I collagen than fibroblasts derived from adipose tissue. Type I collagen is the primary collagen in tendons.

StemCell Technologies

StemCell Technologies, BC, Canada (www.stemcell.com), has signed an agreement to license iPS Academia Japan, Japan’s (www.ips-cell.net) induced pluripotent stem cell technologies. This agreement will enable StemCell Technologies to develop media that are optimized for cellular reprogramming.

Thermo Fisher Scientific

Thermo Fisher Scientific, MA, USA (www.thermofisher.com), introduced the Thermo Scientific HyClone HyCell-STEM and HyCell-STEM-FF stem cell culture media, designed to optimize the expansion rate of human embryonic stem cells and human induced pluripotent stem cells per passage for cell culture applications including cell signaling, drug discovery and therapeutic research. HyCell-STEM is designed for use with stem cells on feeder layer cultures, and HyCell-STEM-FF is designed for stem cells in feeder-free conditions.

■ Achievements

Astellas Pharma

As a part of their collaborative research for kidney regenerative medicine, Astellas Pharma, Japan (www.astellas.com/en) and Center for iPSC Research and Application, Japan (CiRA; www.cira.kyoto-u.ac.jp/e), presented at the International Society for Stem Cell Research’s 11th Annual Meeting, held in Boston, MA, USA, 12–15 June 2013, a method

of differentiating nephron progenitor cells from the nephrogenic intermediate mesoderm [1].

Harvard Bioscience

Harvard Bioscience, MA, USA (HBIO; www.harvardbioscience.com), announced that the ‘InBreath’ tracheal scaffold and bioreactor system manufactured by Harvard Apparatus Regenerative Technology, Inc., MA, USA (HART; www.harvardapparatus.com), its wholly owned regenerative medicine technology subsidiary, were used in the first successful transplant of a regenerated trachea in the USA. The recipient of the implant was a 2-year-old girl. The surgery was also the world’s first successful pediatric regenerated trachea transplant using a synthetic scaffold.

In unrelated news, HBIO announced that HART will not proceed with initial public offer because of unfavorable market conditions. Instead, HBIO is proceeding with the spin-off of HART. All HART’s common stock will be given to HBIO stockholders in a pro-rata, tax-free dividend. Prior spin-off, HBIO is contributing US\$15 million in cash to fund HART’s initial operations.

VistaGen & Duke University

Researchers at Duke University, NC, USA (<http://duke.edu>), combined VistaGen’s, CA USA (www.vistagen.com), human stem cell-derived heart cells with innovative tissue engineering and cardiac electrophysiology technologies to grow what is being called a ‘heart patch’, which mimics the natural functions of native human heart tissue [2]. This heart patch technology is being developed to aid in a better understanding of the biology critical to cardiac tissue engineering, for applications in regenerative cell therapy for heart disease, and as predictive *in vitro* assays for drug rescue and development.

Clinical Trials

Abbott

Abbott, IL, USA (www.abbott.com), has initiated the ABSORB Japan, a randomized controlled clinical trial to evaluate the Absorb™ bioresorbable vascular scaffold (BVS) in patients with coronary artery disease. The results of this trial will support regulatory filings with the Japanese Pharmaceutical and Medical Devices Agency (PMDA; www.pmda.go.jp/english) for approval of Absorb BVS in Japan. The Absorb BVS, a drug-eluting, fully bioresorbable vascular scaffold, is a small mesh tube designed to open a blocked heart vessel, restore blood flow to the heart and then dissolve into the vessel over time, except for two pairs of tiny metallic markers, which help guide placement and remain in the artery to enable physicians to see where the device was placed. Unlike a metallic stent that remains permanently in the body, Absorb BVS is made of polylactide, a naturally dissolvable material that is commonly used in medical implants such as dissolving sutures. Further information about the clinical trial is available at www.clinicaltrials.gov (ID: NCT01844284).

Bioheart

Bioheart, FL, USA (www.bioheart.com) has enrolled and treated the first patients in the ANGEL trial. The trial, fully funded by Bioheart, is being conducted in Mexico at the Hospital Angeles with the Regenerative Medicine Institute (www.regenerativemedicine.mx). The Phase I ANGEL study will provide necessary safety and preliminary efficacy information on adipose-derived stem cells in patients with congestive heart failure. However, the Regenerative Medicine Institute in Tijuana has attracted patient complaints about failed stem cell treatments (www.regenerativemedicinetijuana.com).

Cardio3 BioSciences

Cardio3 BioSciences, Belgium (www.c3bs.com), has treated its first patients in

its CHART-1 European Phase III trial for C-Cure®. The patients, who have been randomly allocated to either the treatment or sham arm of the trial, were treated at the Le Centre Hospitalier Universitaire de Charleroi, Belgium (www.chu-charleroi.be). The trial will recruit a minimum of 240 patients with chronic advanced heart failure of ischemic origin. The primary end point of the trial is a composite end point including mortality, morbidity, 6-min walk test, quality of life, and left ventricular structure and function at 9 months postprocedure. Further information about the clinical trial is available at www.clinicaltrials.gov (ID: NCT01768702).

Cerus

Cerus, CA, USA (www.cerus.com), has initiated patient enrollment in two European Phase III clinical trials for the INTERCEPT Blood System designed to reduce the risk of transfusion-transmitted diseases by inactivating a broad range of pathogens, such as viruses, bacteria and parasites, that may be present in donated red blood cells, platelets or plasma. One trial is being conducted for patients with acute anemia, and a separate trial is being conducted for patients with chronic anemia. Further information about the clinical trials is available at www.clinicaltrials.gov (ID: NCT01716923 and NCT01740531).

Dendreon

Dendreon, WA, USA (www.dendreon.com), presented data from ongoing PROVENGE® and DN24-02 clinical trials at the 49th Annual Meeting of the American Society of Clinical Oncology, 31 May–4 June 2013 in Chicago, IL, USA. PROVENGE® (sipuleucel-T) is autologous peripheral blood mononuclear cells activated with the recombinant antigen *PAP-GM-CSF*. *PAP-GM-CSF* consists of PAP, an antigen expressed in more than 95% of prostate cancers, and GM-CSF, an immune cell activator. Data from an

open-label study demonstrate the presence of existing immunological memory in advanced prostate cancer patients retreated with PROVENGE several years after initial treatment for androgen-dependent prostate cancer in the Phase III PROTECT study. In addition, the retreatment appeared to boost product potency compared with prior treatment. Separately, data from two Phase II studies indicate that PROVENGE can be combined with androgen-deprivation therapy or abiraterone acetate plus prednisone. In addition, the preliminary data demonstrating that the antigen-presenting cell activity of DN24-02 for HER2⁺ urothelial cancer is similar to that of PROVENGE. Further information about the clinical trial is available at www.clinicaltrials.gov (ID: NCT01781390).

Mesoblast

Mesoblast, Australia (www.mesoblast.com), has published preclinical trial results of its allogeneic or ‘off-the-shelf’ mesenchymal precursor cells delivered by intracoronary infusion in acute myocardial infarction [3]. The results of this study form the scientific basis for the current AMICI trial, the first trial to evaluate an allogeneic cellular therapy for acute myocardial infarction delivered by intracoronary infusion. The Phase IIa/IIb trial is recruiting in Europe, Australia and New Zealand. Further information about the clinical trial is available at www.clinicaltrials.gov (ID: NCT01781390).

MiMedx

MiMedx, GA, USA (<http://mimedx.com>), an integrated developer, manufacturer and marketer of patent protected regenerative biomaterials and bioimplants processed from human amniotic membrane, has published results of randomized controlled trial for the EpiFix® wound care allograft [4]. Included in the prospective, randomized, single-center clinical trial were patients with a diabetic foot ulcer of at least 4-week duration without infection

having adequate arterial perfusion. Patients were randomized to receive standard care alone or standard care with the addition of EpiFix. Wound size reduction and rates of complete healing after 4 and 6 weeks were evaluated. After 4 and 6 weeks of treatment, the overall healing rate with application of EpiFix was shown to be 77 and 92%, respectively, whereas standard care healed 0 and 8% of the wounds, respectively. Further information about the clinical trial is available at www.clinicaltrials.gov (ID: NCT01693133).

Northwest Biotherapeutics

Northwest Biotherapeutics, MD, USA (www.nwbio.com), has initiated its Phase III clinical trial with DCVax[®]-L for brain cancer at King's College Hospital, UK (www.kch.nhs.uk). This is one of the first late-stage clinical trials in Europe with active immune therapies. This Phase III trial is for newly diagnosed glioblastoma multiforme, the most common and most lethal form of brain cancer. The trial is already well under way in the USA, with 46 active sites at present, and is expected to enroll an aggregate total of 312 patients in the USA and Europe. DCVax-L mobilizes a cancer patient's whole immune system to attack the full set of biomarker targets

on the tumor. The current standard of care for glioblastoma multiforme includes surgical removal of the tumor, followed by 6 weeks of daily radiation to the brain and daily chemotherapy, followed by monthly chemotherapy. With all of these treatments, the tumors typically recur within approximately 6.9 months, and the patients typically live for approximately 14.6 months. In prior Phase I/II clinical trials, in patients treated with DCVax-L the tumors typically did not recur for 2 years, and the patients typically lived for 3 years. A substantial percentage of patients lived even longer and, to date, two patients have exceeded 10 years. In addition, DCVax-L is nontoxic and is anticipated to cost less than other recent cancer drugs. Further information about the clinical trial is available at www.clinicaltrials.gov (ID: NCT00045968).

Organogenesis

Organogenesis, MA, USA (www.organogenesis.com), announced key findings demonstrating the speed and incidence of wound closure for venous leg ulcer (VLU) patients who were treated with Apligraf[®]. Apligraf contains two layers of human living cells: a layer of differentiated keratinocytes and a layer of fibroblasts in a collagen matrix. When placed on a wound

previously unresponsive to treatment, Apligraf provides cells, collagen matrix and other proteins, and has been demonstrated to promote healing. This retrospective analysis included data from 1489 VLU patients who were treated at wound care facilities across the USA during a 3-year period. The analysis was conducted on treatment records collected from the WoundExpert[®] (Net Health) electronic medical record database. Patients were either treated with Apligraf (n = 1187 patients with 1451 VLUs) or a noninteractive collagen wound dressing (n = 302, which included 350 VLUs). Baseline demographics and wound characteristics, including size and duration, were similar between groups. This comparative effectiveness analysis showed that, when compared with a noninteractive collagen wound dressing, Apligraf healed more wounds (61 vs 46% by 36 weeks; p = 0.01) and healed wounds 44% faster (24 vs 43 weeks; p = 0.01). Analysis of all data over the 3-year period demonstrated a 29% increased probability of healing by with Apligraf (p = 0.01).

Regulations, Approvals & Acquisitions

■ Regulations

Australian Regenerative Medicine Institute

Department of Health and Ageing from Australian Therapeutic Goods Administration (www.tga.gov.au) has released a new Australian code for GMP for human blood and blood components, human tissues and human cellular therapy products [102].

■ Green light

apceth

apceth, Germany (www.apceth.com), has received approval to conduct a clinical cancer trial with its genetically modified, adult mesenchymal stem cells. This is an

entirely new approach for the treatment of advanced types of cancer for which there are currently no effective treatments available. The multicenter, open-label trial will recruit patients suffering from advanced adenocarcinomas of the GI tract. This innovative therapy is based on mesenchymal stem cells harvested from the patients' own bone marrow, which are processed, genetically modified and reinfused into the patient. The stem cells are thus modified specifically to target the tumor and the cytotoxic gene product is selectively activated at the site of the tumor or its metastases to increase local efficacy and to reduce systemic toxicity,

one of the main problems of systemic chemotherapy. This unique principle is also applicable to other cancer types. This clinical trial will be initiated at the University Hospital Grosshadern in Munich, Germany, in the next few weeks in collaboration with experts from the National Center of Tumor Diseases in Heidelberg, Germany (www.dkfz.de/en/nct), and the Karolinska Institute in Stockholm, Sweden (<http://ki.se/?l=en>).

CryoLife

CryoLife, GA, USA (www.cryolife.com), has received Conformité Européenne (CE), mandatory mark that indicates

conformity with legal and technical directives of the EU, for the Hemodialysis Reliable Outflow (HeRO[®]) graft system (www.herograft.com). The HeRO Graft is a proprietary graft-based solution for end-stage renal disease hemodialysis patients with limited access options and central venous stenosis.

Dendreon

The EMA (www.ema.europa.eu), Committee for Medicinal Products for Human Use (CHMP) has adopted a positive opinion recommending that Dendreon's, WA, USA (www.dendreon.com), PROVENGE[®] (sipuleucel-T) be granted marketing authorization in the EU for the treatment of asymptomatic or minimally symptomatic metastatic castrate-resistant prostate cancer in male adults in whom chemotherapy is not yet clinically indicated. The CHMP's recommendation follows a positive recommendation by the EMA's Committee for Advanced Therapy.

Roslin Cells

UK's Medicines Healthcare Products Regulatory Agency (MHRA; www.mhra.gov.uk) has licensed Roslin Cells, UK (www.roslinecells.com), Good Manufacturing Practice (GMP) Cellular Therapy Manufacturing Facility status within the Scottish Centre for Regenerative Medicine, UK, for the manufacture of human cell therapy products. The company has been awarded a Manufacturer's Authorisation for Investigational Medicinal Products (MIA/IMP), which permits the manufacture and release of Advanced Therapy Medicinal Products (ATMPs) for use in clinical trials. In addition, a manufacturer's 'specials' license has been awarded that authorizes the company to manufacture and release ATMPs intended for specific patients.

SanBio

US FDA has approved SanBio's, CA, USA (www.san-bio.com), investigational new drug application for the use of SB623 in

patients suffering from traumatic brain injuries. This approval allows the company to proceed with a Phase I/IIa clinical trial testing the safety and feasibility of the therapy. SanBio has used its proprietary technology to develop three allogeneic stem cell products consisting of cells derived from genetically modified bone marrow stromal cells obtained from healthy adult donors: SB623 for the treatment of stroke, spinal cord injury and Parkinson's disease; SB618 for the treatment of multiple sclerosis and spinal cord injury; and SB308 for the treatment of muscular dystrophy and trauma.

StemCells

Health Canada, ON, Canada (www.hc-sc.gc.ca), has authorized StemCells, CA, USA (www.stemcellsinc.com), to expand into Canada its Phase I/II clinical trial for chronic spinal cord injury. The Phase I/II trial, currently underway in Zurich, Switzerland, is designed to evaluate the safety and preliminary efficacy of the Company's proprietary HuCNS-SC[®] product candidate (purified human neural stem cells) as a treatment for chronic spinal cord injury. Further information about the clinical trial is available at www.clinicaltrials.gov (ID: NCT01321333).

Thermogenesis

ThermoGenesis, CA, USA (www.thermogenesis.com), has received registration approval for its AXP[®] product from China's State Food & Drug Administration (SFDA; <http://eng.sfda.gov.cn/WS03/CL0755>). The product is used to concentrate stem cells from cord blood and, with this approval, the company will immediately initiate commercial distribution of the product in China, one of the world's fastest growing cord blood markets.

■ Pending

RIKEN

Japanese Health Ministry panel decided during a third session held 26 June 2013 to approve the research plan from RIKEN Center for Developmental Biology in Kobe (www.cdb.riken.jp/en/index.html), that will be the world's first clinical application of human induced pluripotent stem cell technologies for regenerative

medicine for humans, on the condition that the scientists closely check the cells earmarked for the transplants for any cancer-inducing genetic mutations and for possible virus contamination during the culture processes. The health minister is expected to issue a formal approval after the decision is presented to a subcommittee of the Health Sciences Council in mid-July.

RNL Bio

RNL Bio, Korea (www.rnl.co.kr/eng/main.asp), has announced that it has filed an IND application with the US FDA to begin clinical trials with its adipose-derived stem cell product, termed RNL-JointStem, for the treatment of osteoarthritis. Assuming approval of the IND, RNL Bio plans to initiate its double-blinded, randomized, positive-control Phase II clinical trial during the third quarter of 2013 in Sugarland, TX, USA. Phase I and Phase II clinical trials of RNL-JointStem have already been completed under the authority of The Ministry of Food and Drug Safety (MFDS), formerly known as the Korea Food and Drug Administration (KFDA).

■ Acquisitions

Regenrys & Altrika

Regenrys, UK (www.regenrys.com), has acquired Altrika, UK (www.altrika.com), which has products for skin regeneration in the treatment of burns and potentially chronic wounds; one of its products, Myskin[®], is used in the National Health Service (NHS) for life threatening burn cases. Altrika also provides bioprocessing and biobanking services to third parties developing advanced cell therapies. No figures for the deal are being disclosed. Regenrys, formerly known as Adiposet, enables a storage and return of the patient's own fatty tissue for breast reconstruction. Its services are provided to both NHS and private healthcare providers and avoid the need for artificial prosthetics in reconstructive surgery.

RTI Biologics & Pioneer Surgical

RTI Biologics, FL, USA (www.rti.com), announced its intent to acquire privately held Pioneer Surgical Technology, MI, USA (www.pioneersurgical.com). Pioneer

manufactures and distributes metal and synthetic products in the orthopedics, biologics, spine, trauma and cardiovascular markets. The acquisition of Pioneer

supports RTI's strategic initiatives to expand its current implant portfolio into metals and synthetics, and to grow direct distribution.

Capital Market & Finances

■ ACell

ACell, MD, USA (www.acell.com), has received the Space Medicine and Related Technologies Commercialization Assistance Program (SMARTCAP) award, given by National Space Biomedical Research Institute, TX, USA (NSBRI), Industry Forum. NSBRI is funded by NASA and includes 12 academic institutions studying the health risks related to long-duration spaceflight and developing the medical technologies needed for long missions. The award will support ACell in the development of innovative new medical devices that address unmet health needs in space and on Earth, specifically in the area of wound care. ACell's leading platform are MatriStem Products, which consist of porcine-derived extracellular matrix, which maintains and supports a healing environment through constructive remodeling, and are available in particle and sheet forms by prescription only. MatriStem medical devices demonstrate the highest constructive remodeling response in a recent study comparing 14 extracellular matrix products designed to aid in surgical procedures [5].

■ bluebird bio

bluebird bio, MA, USA (www.bluebird-bio.com), known for marrying its gene therapy technology with stem cell science, closed off its initial public offer of 6,832,352 shares of common stock at an initial public offer price of US\$17.00 per share, which includes the exercise in full by the underwriters of their option to purchase up to 891,176 additional shares of common stock. All of the shares in the offering were offered by bluebird bio. The company's common stock is listed

on the NASDAQ Global Select Market under the trading symbol 'BLUE.' J.P. Morgan Securities LLC (www.jpmorgan-securities.com) and BofA Merrill Lynch (<http://corp.bankofamerica.com>) are acting as joint book-running managers for the offering.

■ Cardio3 BioSciences

Cardio3 BioSciences, Belgium (www.c3bs.com), launched its initial public offer on New York Stock Exchange (NYSE) Euronext in Brussels and Paris (www.nyx.com), to subscribe for up to 1,300,000 new ordinary shares, which can be increased by a maximum of 15% to 1,495,000. The indicative price range of the offering has been set at a minimum of US\$21.7 (EUR€16.65) and a maximum of US\$24.8 (EUR€9.00) per share.

■ Cellular Dynamics International

Cellular Dynamics International, WI, USA (www.cellulardynamics.com), has filed a registration statement with the US Securities and Exchange Commission, (www.sec.gov), relating to the proposed initial public offer of its common stock. The offering will be made only by means of a prospectus and JP Morgan Securities LLC (www.jpmorgansecurities.com) is acting as the sole book-running manager for the offering.

■ Fibrocell

Fibrocell Science's, PA, USA (www.fibrocellscience.com), common stock has been approved for listing on the NYSE Market, (www.nyse.com) under the ticker symbol 'FCSC', which will increase the awareness of the FDA-approved product LAVIV® (azficelT), as well as their pipeline for the

treatment of restrictive burn, vocal cord and acne scarring, and state-of-the-art medicines in development for rare genetic skin diseases.

■ Kadimastem

Kadimastem, Israel (www.kadimastem.com), focusing on the development and industrial commercialization of products based on human embryonic stem cells, closed its initial public offer on the Tel Aviv Stock Exchange (Israel). The tender, which included 3.1 million shares and two option series, recorded demands in the scope of approximately US\$5.5 million. The tender price closed at US\$1.81 per share. The first option series is for a period of 2 years from the date of the offering. The additional series is for a period of 4 years from the date of the offering. The company announced that the capital raised will be used to expand its current activities.

■ ReproCELL

ReproCELL, Japan (www.reprocell.com), has received formal approval from the Osaka Stock Exchange (OSE; Japan) for listing on the Japan Association Of Securities Dealers Automated Quotation (JASDAQ; www.ose.or.jp/e/jasdaq) Market Growth and is trading under the OSE listing code 4987. The shares went untraded for 2 days after listing on JASDAQ on 26 June 2013 since buy offers outnumbered sell orders by as much as ten to one. The shares traded on the first day at US\$183.63 (¥18,300) at the close in Tokyo, 472% above its initial public offer price of US\$32.11 (¥3200). This is the biggest jump for an initial public offer over US\$10 million in Japan since 1999.

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.

No writing assistance was utilized in the production of this manuscript.

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