Latest developments in the field of stem cell research and regenerative medicine compiled from publicly available information and press releases from nonacademic institutions 1 February–31 March 2015

Business development

Collaborations, partnerships & alliances

Co-development agreement: Merck Serono & Otsuka

Merck (Germany; www.merckgroup.com) subsidiary Merck Serono (Germany; www.merckserono.com) has amended its development and license deal with Opexa Therapeutics (TX, USA; www.opexatherapeutics.com) for Tcelna (imilecleucel-T), handing over US\$3 million to further support an ongoing trial with the personalized immunotherapy for multiple sclerosis. Merck's payment will help fund the current Phase IIb clinical study assessing Tcelna for patients with secondary progressive multiple sclerosis, as well as support planning of potential late-stage trials. Under their original 2013 deal, Merck Serono paid Opexa a US\$5 million upfront fee for the option to exclusively license Tcelna – a potential first-in-class personalized therapy, which has received USA fast-track designation for the treatment of multiple sclerosis. Merck's option can be exercised prior to or upon completion of the ongoing midstage study, top-line data from which is expected in the second half of 2016. If this occurs, Merck will pay Opexa another US\$25 million (or US\$15 million, depending upon whether certain conditions are met) for worldwide development and commercial rights excluding Japan, and fund its further development.

Collaboration agreement: ARM & FIRM

The Alliance for Regenerative Medicine (ARM; <http://alliancerm.org>), the international organization representing the regener-

ative medicine and advanced therapies field, has entered into a Memorandum of Understanding with Japan's Forum for Innovative Regenerative Medicine (FIRM; <http://firm.or.jp/en>). FIRM is a Tokyo-based trade association that establishes advanced therapies industry-led partnerships with governments, academia, research institutions and the private sector to further research and promote a stable and welcoming business environment. According to the terms of the Memorandum, ARM and FIRM will be granted reciprocal, nonvoting membership in the other's organization and will be responsible for reporting on pertinent regulatory trends. The organizations will also have the opportunity to participate in the other's events and conferences as presenters and panelists, and will have an observation role in the other's board and membership meetings.

Collaboration agreement: AstraZeneca & Harvard Stem Cell Institute

AstraZeneca (UK; www.astrazeneca.co.uk) entered into a 5-year research collaboration with the Harvard Stem Cell Institute (MA, USA; <http://hsci.harvard.edu>) to adapt a technique that creates human pancreatic β -cells from stem cells for use in screens of AstraZeneca's compound library in the search for new treatments for diabetes. AstraZeneca will provide funding for a team of investigators at Harvard Stem Cell Institute led by Dr Melton as well as establishing an in-house team in Mölndal, Sweden, dedicated to the collaboration. Scientists from each organization will work together to understand the biology behind the loss of

Dusko Ilic

Stem Cell Laboratories, Guy's Assisted Conception Unit, Division of Women's Health, King's College London Faculty of Life Sciences & Medicine, London, UK
dusko.ilic@kcl.ac.uk

human β -cell function and mass in diabetes, and to screen compounds against the cells produced to search for potential new medicines that could restore β -cell activity in diabetic patients.

Collaboration agreement: Eppendorf & Florida State University

A collaboration between Eppendorf (Germany; www.eppendorf.com) and Florida State University (FL, USA; www.fsu.edu) has successfully shown the feasibility of large-scale expansion of human mesenchymal stromal/stem cells (MSC) using the company's proprietary Fibracel[®], a packed-bed 3D matrix, using a CelliGen[®] 310 bioreactor at approximately 2-l scale.

Collaboration agreement: inStem & L'Oréal

The Institute of Stem Cell Biology and Regenerative Medicine (inStem; India; <http://instem.res.in>) and L'Oréal (France; www.loreal.com) have entered into a collaborative agreement for the next 3 years to initiate research on different aspects of skin biology. A major objective of this collaboration would be to study the molecular mechanisms and signaling pathways involved in the cell biology of skin homeostasis. L'Oréal will share its active ingredients for evaluation and validation of these concepts.

Licensing agreement: Ocata & Allele

Ocata Therapeutics (MA, USA; www.ocata.com), formerly known as Advanced Cell Technology (MA, USA; www.advancedcell.com), has entered into a definitive agreement with Allele Biotechnology & Pharmaceuticals (CA, USA; www.allelebiotech.com) to access Allele's proprietary technology for generating human-induced pluripotent stem cells (iPSC) [1].

Manufacturing agreement: ImmunoCellular & PharmaCell

ImmunoCellular Therapeutics (the Netherlands; www.imuc.com) established an agreement with PharmaCell (The Netherlands; www.pharmacell.nl) to provide contract manufacturing services for the European production of ICT-107, a dendritic cell-based cancer immunotherapy in development as a potential treatment for glioblastoma. This agreement with PharmaCell is designed to enable ImmunoCellular to access Phase III supplies of ICT-107, manufactured with ImmunoCellular's commercial-ready production.

Manufacturing agreement: Lonza & TiGenix

Lonza (Switzerland; www.lonza.com) has entered into an agreement for the supply of Belgian biopharmaceutical firm TiGenix's (Belgium; www.tigenix.com) product Cx601, indicated to treat complex perianal fistulas in Crohn's disease patients. As part of the deal, Lonza will manufacture material for the Phase III trial of Cx601 in the USA at Lonza's cell therapy production facility in Walkersville, MD, USA. TiGenix is focused on developing and commercializing new therapeutics from allogeneic expanded adipose-derived stem cells (eASCs) in inflammatory and autoimmune diseases. Cx601 is a locally injected suspension of allogeneic eASCs and is currently in Phase III of clinical development in Europe. Further information about that clinical trial in the USA is available at <http://clinicaltrials.gov> (ID: NCT01372969).

Manufacturing & distribution agreement: Accellta & StemCell Technologies

Accellta (Israel; www.accellta.com) has granted exclusive worldwide rights to StemCell Technologies (BC, Canada; www.stemcell.com) for manufacturing and distribution of medium for culturing pluripotent stem cells in suspension under feeder-free, nonadherent conditions.

Partnership agreement: Athersys & Chugai

Athersys (OH, USA; www.athersys.com) and Chugai Pharmaceutical (Japan; www.chugai-pharm.co.jp/english) have announced a partnership and license agreement to exclusively develop and commercialize Mul-

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tiStem® cell therapy for ischemic stroke in Japan. As part of the collaboration, Chugai will be responsible for the development and commercialization of MultiStem for ischemic stroke in Japan, and Athersys will have responsibility for product supply. Under the financial terms of the agreement, Athersys will receive an up-front cash payment of US\$10 million from Chugai and would receive additional payments as the program is further advanced. Athersys is eligible to receive milestone payments from Chugai of up to US\$45 million upon the successful achievement of certain development and regulatory milestones, and sales milestones of up to US\$150 million. Athersys would also receive from Chugai tiered, double-digit royalties on any net sales, as well as payments for product supplied to Chugai. In Athersys' ongoing Phase II clinical study, it is evaluating the administration of MultiStem cell therapy to patients who have suffered an ischemic stroke. Further information about that clinical trial in the USA is available at <http://clinicaltrials.gov> (ID: NCT01436487).

Launching new projects, products & services Cardio3 BioSciences

Cardio3 BioSciences (C3BS; Belgium; www.c3bs.com) confirmed plans to open a new USA-based manufacturing facility in Rochester, Minnesota. The facility will support the Company's current and anticipated manufacturing needs in the USA for both the Phase III clinical trial evaluating lead cardiovascular product candidate C-Cure® (CHART-2), and its recently acquired CAR T-cell therapies' portfolio. The facility will also serve as a base for the Company's research and clinical collaboration with Mayo Clinic, also based in Rochester. C-Cure is an autologous cellular therapy for the treatment of congestive heart failure that is based on the Company's proprietary cardiopoiesis platform, initially developed using fundamental research and proprietary technology from the Mayo Clinic. The 11,000-square feet (1000 m²) facility is located in the Minnesota Bio Business Center in downtown Rochester and will initially primarily be used to manufacture C-Cure for use in CHART-2, the USA Phase III trial. Cardio3 BioSciences will receive nondilutive funding from The Minnesota Department of Employment and Economic Development (DEED) and the Minnesota Job Creation Fund once it completes its investment and hiring goals.

City of Hope

City of Hope officially opened the Alpha Clinic for Cell Therapy and Innovation (CA, USA; <http://cityofhope.org/alpha-clinic-for-cell-therapy>) on 19 March, funded by a US\$8 million, 5-year grant from the California Institute for Regenerative Medicine (www.cirm.ca.gov) that will be supplemented by matching

funds from City of Hope. It will combine the uniquely patient-centered care for which City of Hope is known with the most innovative, stem cell-based therapies being studied to date. The approach is expected to revolutionize the treatment of not only cancer, but also AIDS and other life-threatening diseases

WuXi

WuXi PharmaTech (China; www.wuxiapptec.com) will soon begin construction of a new, 145,000-square feet (13,470 m²) current Good Manufacturing Practice (cGMP) facility in Philadelphia for the manufacture of cell therapy products. This facility is designed for cell therapy products that contain viral vectors such as chimeric antigen receptor T-cell (CAR T cell) therapies. CAR T cells are T cells harvested from a patient's body, engineered to target specific cancers, and then reintroduced into the body.

Achievements

BMDW & WMDA

Bone Marrow Donors Worldwide (BMDW; www.bmdw.org) and the World Marrow Donor Association (WMDA; www.wmda.info) announced that a record 25 million people worldwide are currently listed as potential volunteer marrow donors in hopes of saving the lives of those battling life-threatening blood cancers and diseases. The significant milestone gives greater hope to searching patients, caregivers and healthcare professionals around the world. BMDW was created in 1989 as a collaborative effort of eight countries and has grown to a community of 53 countries that are working together to achieve a centralized file of all potential volunteer marrow donors worldwide. This resource is crucial for patients in need of a blood stem cell transplant, because in nearly 50% of blood stem cell transplants, the donor and the patient come from different countries. BMDW works closely with the WMDA – an association responsible for establishing consistent, high-quality standards for worldwide marrow donor registries – and provides a comprehensive list of potential marrow donors and donated umbilical cord blood units, primarily from WMDA member registries and cord blood banks. The BMDW global database is easily accessible to physicians to search on behalf of their patients in need of a blood stem cell transplant.

Cellular Dynamics International

Cellular Dynamics International (WI, USA; www.cellulardynamics.com) has manufactured, under cGMP, iPSC lines from two human leukocyte antigens (HLA) 'superdonors' providing a partial HLA match to 19% of the USA population. HLA superdonors are individuals whose genetic HLA profiles make their cells or tissues

more compatible for donation to unrelated patients – a concern that arises with organ or tissue transplantation and potential rejection. As the first announced HLA superdonor master cell bank in the world, and the first produced under cGMP, these cell lines will enable a new area of cell therapy research using HLA matching. Company plans to continue to expand this master stem cell bank with the collection of additional donor cell lines to cover 95% of the USA population. Cellular dynamics manufactured the HLA superdonor cell lines from blood samples collected from eligible anonymous donors.

Cynata

Cynata Therapeutics (Australia; www.cynata.com) has achieved a world first breakthrough in the manufacture of stem cells and is now set to scale up manufacturing of its MSCs for therapeutic use. The Company's lead platform technology – a novel stem cell manufacturing process known as Cymerus™ – has now been successfully validated at Waisman Biomanufacturing (WI, USA; gmpbio.org). This state-of-the-art stem cell manufacturing process is capable of producing MSCs for therapeutic application, consistently, efficiently and economically, in a cGMP production environment. Importantly, the Cymerus process uses

an effectively limitless starting material – a bank of iPSC – and a patent-protected process to derive MSCs for commercial use. This is a world-first breakthrough that sets Cymerus apart from all existing methods of MSC production, which require a continuous supply of new tissue donations. Cynata expects to be able to produce all of the MSCs it will ever need from a single iPSC bank, derived from a single blood donation. Consequently, there will be no need to repeatedly source, screen and test new donors and issues with donor-to-donor variability will not arise. Further, the use of an essentially limitless starting material means that it will not be necessary for Cynata to excessively expand MSCs in culture in order to generate the vast numbers of cells required to provide commercially viable treatments for major diseases. All of these advantages will result in significantly reduced costs. A Phase I human clinical trial of the Cymerus stem cell technology is currently in the planning stage, with discussions underway with regulatory authorities to ascertain and clarify the likely regulatory path for this cutting-edge therapeutic product. The proposed clinical study is intended to examine the impact of these manufactured cells on patients affected by graft-versus-host disease (GvHD).

Clinical trials

apceth

apceth (Germany; www.apceth.com) successfully completed the Phase I and initiated the Phase II part of its ongoing monocentric Phase I/II clinical trial TREAT-ME 1 with the engineered cell therapeutic product Agenmestencil-T, at the Klinikum Grosshadern in Munich. To the company's knowledge, this is the first time that a genetically engineered MSC treatment has successfully completed a Phase I clinical trial and been approved to initiate a Phase II trial. The first patient in the Phase II trial has already been treated. The completed Phase I trial included six patients suffering from advanced-stage gastrointestinal adenocarcinomas (three colorectal, two pancreatic and one cholangiocellular carcinoma). Analysis confirmed that the infusion of the engineered cells and the treatment was safe and tolerable.

Asterias

BioTime's (CA, USA; www.biotimeinc.com) subsidiary Asterias Biotherapeutics (MA, USA; www.ocata.com), announced today that Shepherd Center (GA, USA; www.shepherd.org), has commenced enrollment for the Phase I/IIa clinical trial of AST-OPC1 (oligodendrocyte progenitor cells) in newly injured patients with sensory and motor complete cervical spi-

nal cord injury. The Phase I/IIa trial follows the successful completion of the Phase I trial run by Geron (CA, USA; www.geron.com), which met its primary end points of safety and feasibility when administered to five patients with neurologically complete, thoracic spinal cord injury. Shepherd Center was a site in the Phase I study and enrolled two of the five subjects in that study. Asterias intends to initiate enrollment for the Phase I/IIa trial at up to seven additional sites in the coming months. The Phase I/IIa clinical trial is designed to assess safety and activity of escalating doses of AST-OPC1 for complete cervical spinal cord injury. The trial will be an open-label, single-arm study testing three escalating doses of AST-OPC1 in patients with subacute, C-5 to C-7, neurologically complete cervical SCI. These individuals have essentially lost all sensation and movement below their injury site with severe paralysis of the upper and lower limbs. AST-OPC1 will be administered 14–30 days postinjury. Patients will be followed by neurological exams and imaging methods to assess the safety and activity of the product. The company plans to seek US FDA concurrence to increase the robustness of the proof of concept in the Phase I/IIa clinical trial by expanding enrollment from 13 patients to up to 40 patients. The company believes these changes will increase the statistical confidence

of the safety and efficacy readouts, reduce the risks of the AST-OPC1 program and position the product for potential accelerated regulatory approvals. Asterias has received a Strategic Partnerships Award grant from the California Institute for Regenerative Medicine, which provides US\$14.3 million of nondilutive funding for the Phase I/IIa clinical trial and other product development activities for AST-OPC1. Further information about this clinical trial are available at <http://clinicaltrials.gov> (ID: NCT02302157).

BioLineRx

BioLineRx (Israel; www.biolinerx.com) announced successful top-line results from the Phase I safety and efficacy study of its lead clinical candidate, BL-8040, as a novel approach for mobilization and collection of bone-marrow stem cells from the peripheral blood circulation. All safety and efficacy end points were met, showing that treatment with BL-8040 as a single agent was safe and well tolerated at all doses and resulted in efficient stem cell mobilization and collection in all study participants. Importantly, the results support BL-8040 as 1-day, single-dose collection regimen, which is a significant improvement upon the current standard of care. Robust stem cell mobilization was evident in all treated participants, across the different doses tested, supporting a novel approach to stem cell collection. After a single administration, BL-8040 enabled collection of a yield of stem cells that exceeds the number required to support a transplant in all treated participants, following only one collection procedure. BL-8040 is a short peptide, which functions as a high-affinity antagonist for CXCR4, a chemokine receptor that is directly involved in tumor progression, angiogenesis, metastasis and cell survival. BL-8040 also mobilizes cancer cells from the bone marrow and may therefore sensitize these cells to chemo- and bio-based anticancer therapy. BL-8040 was licensed by BioLineRx from Biokine Therapeutics and was previously developed under the name BKT-140.

Bone Therapeutics

Bone Therapeutics (Belgium; www.bonetherapeutics.com) announced that the first four patients in the Phase IIA proof-of-concept study for spinal fusion procedures have been treated with Bone Therapeutics' allogeneic osteoblastic cell therapy product, ALLOB®. This pilot Phase IIA study will enroll 16 patients with symptomatic degenerative lumbar disc disease who require interbody fusion surgery (a type of spinal fusion surgery that involves placement of fusion implants and bone grafts into the area between two vertebral bodies). Patients will be treated with a single dose of ALLOB® combined with bioceramic granules to achieve bone

formation and fusion of the vertebral bodies. Safety and efficacy of this treatment will be assessed over 12 months, using clinical and radiological evaluation. Further information about this clinical trial is available at <http://clinicaltrials.gov> (ID: NCT02205138).

Cell Cure

BioTime's (CA, USA; www.biotimeinc.com) subsidiary Cell Cure Neurosciences (Israel; www.cellcure-neurosciences.com) opened the clinical trial of OpRegen® titled "Phase I/IIa dose escalation safety and efficacy study of human embryonic stem cell (hESC)-derived retinal pigment epithelium cells transplanted subretinally in patients with advanced dry-form age-related macular degeneration with geographic atrophy" at Hadassah University Medical Center in Jerusalem, Israel. Patient enrollment is expected to begin shortly. OpRegen comprises animal product free retinal pigment epithelial (RPE) cells with high purity and potency. Cell Cure also announced that the option granted to Teva Pharmaceutical Industries (Israel; www.tevapharm.com) under a Research and Exclusive Option Agreement of 7 October 2010 to license-in rights to its OpRegen product has expired without having been exercised by Teva. Cell Cure will therefore be continuing the clinical development of OpRegen on its own and pursuing discussions with other potential strategic partners. Further information about this clinical trial is available at <http://clinicaltrials.gov> (ID: NCT02286089).

Cellerant

Cellerant Therapeutics (CA, USA; www.cellerant.com) announced that patient dosing has commenced in its multi-center, open-label, randomized controlled Phase II clinical trial of CLT-008, a first-in-class, allogeneic, cellular therapy, in *de novo* acute myeloid leukemia patients receiving induction chemotherapy. CLT-008 is a unique, off-the-shelf, cryopreserved, cell-based therapy that contains human myeloid progenitor cells derived from adult hematopoietic stem cells that have the ability to mature into functional granulocytes and platelets *in vivo*. Cellerant's CLT-008 development program, including this Phase II clinical trial in AML patients, and the nonclinical studies required for approval in treating acute radiation syndrome, is funded under a US Government contract awarded on 1 September 2010 and valued at up to US\$188 million. Further information about this clinical trial is available at <http://clinicaltrials.gov> (ID: NCT02282215).

NeuralStem

Neuralstem, Inc. (MD, USA; www.neuralstem.com) announced top-line data from the Phase II

trial of NSI-566 spinal cord-derived neural stem cells under development for the treatment of amyotrophic lateral sclerosis (ALS). The study met primary safety end points. The maximum tolerated dose of 16 million transplanted cells and the surgery was well tolerated. Secondary efficacy end points at 9 months postsurgery indicate a 47% response rate to the stem cell treatment, as measured by either near-zero slope of decline or positive slope of ALS functional rating scale (ALSFERS) score in seven out of 15 patients and by either a near-zero decline, or positive strengthening, of grip strength in seven out of 15 patients. Grip strength is an indicator of direct muscle strength of the lower arm. ALSFERS is a standard clinical test used to evaluate the functional status of ALS patients. The average ALSFERS score for responders at 9 months after treatment was 37. Nonresponders scored an average of 14. These scores represent 93%, versus 35%, of the baseline score retained, respectively, by the responders versus nonresponders at 9 months, which is a statistically significant difference. As measured by an average slope of decline of ALSFERS, responders' disease progression was -0.007 point per day, while nonresponders' disease progression was -0.1 per day, which was again statistically significant. Lung function as measured by

Seated Vital Capacity shows that responder patients remained within 94% of their starting scores, versus 71% for nonresponder patients. The trial met its primary safety end points. Both the surgery and cells were well tolerated, with one patient experiencing a surgical serious adverse event. Further information about this clinical trial are available at <http://clinicaltrials.gov> (ID: NCT01730716).

Ocata

Ocata Therapeutics (MA, USA; www.ocata.com), formerly known as Advanced Cell Technology (MA, USA; www.advancedcell.com), has completed dosing of its Phase I/II studies for dry age-related macular degeneration (dry AMD) and Stargardt's Macular Degeneration. A total of 38 patients have been safely dosed. The 200,000 cell cohort, the highest level planned was successfully completed, paving the way for the next phase of the programs. Ocata previously announced that it has been granted Advanced Therapy Medicinal Product (ATMP) designation for its RPE therapy for macular degeneration. The SMD program has orphan status both in Europe and the USA. Further information about these clinical trials is available at <http://clinicaltrials.gov> (ID: NCT01344993 and NCT01345006).

Regulations, approvals, acquisitions...

Green light

Neurotech

US FDA gave a green light to Neurotech Pharmaceuticals (RI, USA; www.neurotechusa.com) to proceed with its investigational new drug application to conduct a Phase II clinical study of NT-503 encapsulated cell therapy (ECT) for the treatment of recurrent subfoveal choroidal neovascularization secondary to age-related macular degeneration (wet AMD). The Phase II, randomized, active-controlled, masked study will commence immediately and enroll 150 patients. The safety and efficacy of one NT-503 ECT implant will be compared with aflibercept intravitreal injections every 8 weeks in patients who have been treated with at least three anti-VEGF injections and still have active disease. Patients will be followed for 2 years with a 12-month interim assessment. ECT is an intravitreal implant that houses a proprietary retinal pigment epithelial cell line genetically engineered to produce several therapeutically active biologics for at least 2 years. NT-503 is a novel VEGF receptor protein that is continuously produced by the ECT platform.

ViaCyte

ViaCyte (CA, USA; www.viacyte.com), a privately held regenerative medicine company with the first hESC-

derived islet replacement therapy for the treatment of diabetes in clinical trials, has received a no objection letter from Health Canada providing clearance to proceed with sites in Canada for the company's Phase I/II clinical trial of its VC-01TM product candidate. The VC-01 product candidate is currently being evaluated in patients with Type 1 diabetes who have minimal-to-no insulin-producing β -cell function. The location and enrollment start date of the first Canadian clinical trial site have not yet been disclosed. Further information about the ongoing clinical trial in the USA is available at <http://clinicaltrials.gov> (ID: NCT02239354).

Red light

WARF

A 9-year legal challenge to human embryonic stem cell patents ended, when the Supreme Court declined to hear the case. The decision means the Wisconsin Alumni Research Foundation (WARF; WI, USA; www.warf.org), will get to keep its patent rights for the hESC, which were discovered in 1998 by University of Wisconsin – Madison scientist James Thompson [2]. WARF maintains it has the right to license use of human embryonic stem cells, because Thompson developed the methods to isolate them from embryos, which had not been

previously done even though the derivation is an obvious extension of methods used to derive nonprimate embryonic stem cells, and therefore not patentable. However, the challengers succeeded in preventing WARF from gaining rights over iPSC. Two public interest groups, Consumer Watchdog (CA, USA; www.consumer-watchdog.org) and the Public Patent Foundation (NY, USA; www.pubpat.org), challenged the patents in 2006, and in 2007 succeeded in narrowing WARF's claims to exclude the iPSC. The groups continued the challenge on the grounds that as a product of nature, hESC are not patentable. The US Patent and Trade Office turned down that challenge, and the case reached the Supreme Court last year. By not hearing the case, the Supreme Court let that decision stand.

Acquisitions

Actavis & Allergan

Shareholders of Actavis (Ireland; www.actavis.com) and Allergan (CA, USA; www.allergan.com) approved all proposals related to Actavis's planned acquisition of Allergan. The deal, valued at US\$66 billion, is expected to close in the second quarter. The combined company would be one of the world's largest drug makers by sales, with about US\$23 billion in sales, led by Allergan's antiwrinkle treatment Botox. Actavis's shares, up nearly 38% over the past 12 months, edged up to US\$290.17 in recent after-hours trading, while Allergan's shares, up 80% over the past 12 months, edged up to US\$233.90.

FujiFilm & CDI

FujiFilm (Japan; <http://www.fujifilmholdings.com/en/index.html>) will acquire Cellular Dynamics International (WI, USA; www.cellulardynamics.com), via an all-cash tender offer to be followed by a second step merger. FujiFilm aims to acquire all issued and outstanding shares of Cellular Dynamics' common stock for US\$16.5 per share or approximately US\$307 million (on a fully diluted basis). The offer represents a premium of 108% to Cellular Dynamics' closing price on 27 March. Upon completion of the transaction, Cellular Dynamics' will continue to run its operations in Madison, Wisconsin and Novato, California as a consolidated subsidiary of FujiFilm.

Kite & TCF

Kite Pharma (CA, USA; www.kitepharma.com) has acquired privately held T-Cell Factory (TCF; The Netherlands) for US\$22.5 (€1.0) million million) upfront, and renamed it Kite Pharma EU, in a deal designed to establish a European presence for the buyer and strengthen its T-cell receptor (TCR) gene therapy product platform. TCF has focused on discovery and development of tumor-specific TCRs for broad use in cancer treatment based on its TCR-GENERator™ platform. TCRs allow targeting of tumor antigens found inside cancer cells, as well as surface antigens. Kite agreed to make the upfront payment, of which US\$4.0 (€0.8) million will be paid in Kite stock, as well as an undisclosed sum in payments tied to achieving clinical, regulatory and sales milestones relating to TCR-based product candidates.

Orgenesis & MaSTherCell

Orgenesis (NY, USA; www.orgenesis.com) is acquiring MaSTherCell (Belgium; www.masthercell.com), a contract development and manufacturing organization. Orgenesis bought all issued and outstanding shares of MaSTherCell in exchange for US\$24.593 million in shares of the acquiring company's common stock. Orgenesis said MaSTherCell proved to be an attractive acquisition target because of its process development capabilities and fully closed and tightly controlled GMP systems required to deliver commercial-scale manufacturing. Before the acquisition, the two companies had already been working together under a strategic manufacturing agreement.

Valeant & Dendreon

Valeant Pharmaceuticals International (QC, Canada; www.valeant.com) has purchased bankrupt Dendreon (WA, USA; www.dendreon.com) and its prostate cancer vaccine Provenge® (sipuleucel-T) for US\$415 million [3]. Dendreon filed for Chapter 11 bankruptcy protection in November 2014 battered by the failure of Provenge, which cost US\$93,000 for a course of treatment, to make a dent in the prostate cancer markets. Provenge had sales of around US\$300 million last year.

Capital market & finances

Athersys

Athersys (OH, USA; www.athersys.com) has been awarded a grant from Innovate UK (www.gov.uk/government/organisations/innovate-uk), which will support a Phase IIa clinical study evaluating the administration of MultiStem® cell therapy to acute

respiratory distress syndrome patients. The grant is expected to provide up to approximately US\$3.0 (£2.0) million in support over the course of the study, which will be conducted by Athersys' affiliate at leading clinical sites in the UK Therapy Catapult (<https://ct.catapult.org.uk>).

Coriell

Coriell Institute for Medical Research (NJ, USA; www.coriell.org) has won a US\$14 million grant through an open competition from the National Institute of General Medical Sciences, a component of the NIH. The 5-year award supports the NIGMS Human Genetic Cell Repository at Coriell, a dynamic collection of more than 11,300 cell lines and 5700 DNA samples representing a variety of disease states, chromosomal abnormalities and healthy individuals across several distinct human populations.

LCT

Living Cell Technologies (New Zealand; www.lctglobal.com) and its 50% owned joint venture Diatranz Otsuka Limited (New Zealand; www.dolglobal.com) has adopted a new development strategy for DIABECCELL®. Diatranz will partner with its other 50% shareholder, Otsuka Pharmaceutical Factory (Japan; www.otsukakj.jp/en/) to support the development and launch of DIABECCELL in USA. Diatranz retains a royalty-free right to commercialize DIABECCELL outside USA and Japan. Diatranz's funding requirements have reduced as a result of the new development strategy and the Otsuka loan facility has been amended to provide funding of up to US\$20 (NZ\$28) million. The new strategy will mean that Diatranz and Otsuka will focus on developing a DIABECCELL product that will meet US FDA regulatory requirements. Approval by the FDA will facilitate approval for the product across the rest of the world.

Plasticell

Innovate UK (www.gov.uk/government/organisations/innovate-uk) will provide a grant of approximately US\$2.0 (GB£1.3) million to a research consortium led by Plasticell (UK; www.plasticell.co.uk) for a project

entitled 'Ex vivo expansion of cord blood and bone marrow stem cells'. The consortium includes the University of Oxford and the Cell Therapy Catapult (<https://ct.catapult.org.uk/>). Using CombiCult®, Plasticell has tested millions of combinations of cell culture components to develop cord blood expansion media which amplify stem cells by up to 100-fold. This grant will allow the consortium to develop a clinically compliant process to expand cord blood stem cells *ex vivo* using Plasticell's media.

Semma

Semma Therapeutics (MA, USA; www.semma-tx.com), a company developing a cell therapy for Type 1 diabetes, has closed a US\$44 million Series A comprising equity financing and strategic funding. The Series A financing is led by MPM Capital (CA, USA; www.mpmcapital.com), with Fidelity Biosciences (MA, USA; www.fidelitybiosciences.com), ARCH Venture Partners (IL, USA; www.archventure.com), and Medtronic (MN, USA; www.medtronic.com) participating. Alongside the equity financing, Semma entered into an undisclosed agreement with Novartis Pharmaceuticals (Switzerland; www.novartis.com). Semma is building on the scientific foundation laid by the work of Doug Melton's group from Harvard [4].

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