Commercial insight: cell and gene therapy

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Providing a critical overview of the sector's commercial developments – M&As, licensing agreements & collaborations, financial results, IPOs and clinical/regulatory updates, with commentary from our Expert Contributors.

GENE THERAPY
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GENE THERAPY: This month sees continued intense activity in CRISPR-Cas9 and related technologies for gene editing. In the race to initiate the first clinical trial using the CRISPR-Cas9 approach, it looks like a team of Chinese scientists based at Sichuan University will be the first to the start line, in a phase 1 safety study targeting PD-1 in patients with lung cancer. In addition, collaborative agreements between industry and academia continue to flow, with Evotec and Editas both signing agreements with academic partners (MIT/Harvard and San Raffaele Telethon Institute for Gene Therapy respectively) in the field of gene editing. There are a lot of bets being placed on gene editing, although it remains to be seen whether any will translate to meaningful clinical efficacy with acceptable safety.

CELL THERAPY: It was a tumultuous month for Juno Therapeutics after the FDA announced a clinical hold on its Phase 2 study of JCAR015 in adult patients with relapsed/refractory B cell ALL. Juno reported three patient deaths, two the week prior and one in May. All three of the patients died following cerebral edema after administration of JCAR015 in

combination with fludarabine as a preconditioning agent. As would be expected the market didn't take overly well to the news and the stock crashed more than 30% in the ensuing days of trading. Certainly the late reporting on the first patient death was a surprise to many, though it seemed some investors were willing to move on. Following a press release five days later, announcing the clinical hold was being lifted, the stock rebounded. However, ongoing investigations into management's dealing with the situation are capping the stock price for the moment. Industry and investors will now wait to see whether it will be determined that Juno misled investors in claiming JCAR015's safety profile was looking good, amidst a patient death that went unreported.

3 PATIENTS DIE IN ZIOPHARM'S PHASE 1 GENE THERAPY TRIAL

Ziopharm Oncology, a Boston-based biopharmaceutical company specialized in developing immunotherapies for the treatment of cancer, has confirmed 3 patient deaths in their Phase 1 gene therapy trial for glioblastoma. This single-arm, open-label multicenter study is designed to evaluate the safety and tolerability of a single tumor injection of Ad-RTS-hIL-12 in combination with Veledimex for the treatment of recurrent or progressive glioblastoma or grade III malignant glioma.

Ad-RTS-hIL-12 is an adenovirus vector engineered for the controlled expression of interleukin 12 (IL-12). Presence of IL-12 in the body enhances the ability of body's immune system to kill tumor cells and interferes with blood flow to the tumor. Ad-RTS-hIL-12 has been granted Orphan Drug Designation by the US FDA for the treatment of patients with malignant glioma. Secondary objectives of the study include determination of maximum tolerated dose, immune responses and assessment of biologic responses.

Ziopharm's study included three cohorts of patients; the first cohort of seven patients received 20 mg doses of veledimex, the second cohort of six patients received 40 mg doses of veledimex, and the third cohort, for which the enrolment is currently ongoing, receives 30 mg doses of veledimex. The first patient died 6.7 months following a 20 mg dose; the second patient died 3.9 months after treatment with a 40 mg dose; and the third patient died of an intracranial haemorrhage, 15 days after starting on a 30 mg dose of the gene therapy. Ziopharm has yet to report the third death to the FDA and is currently collecting and analyzing information for the submission.

Dr. Laurence Cooper, CEO of Ziopharm commented following the final death: "This is an isolated case, and there have been no reported related instances of brain hemorrhage in any previous cohort or prior studies with Ad-RTS-hIL-12 + veledimex. Enrollment remains open in the study, and we will be discussing with our Safety Review Committee the appropriate course of action."

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ADAPTIMMUNE'S T-CELL THERAPY GAINS ACCESS TO EMA'S PRIME SUPPORT

Adaptimmune Therapeutics, a clinical-stage biopharmaceutical company specialized in developing cancer immunotherapy products based on its Specific Peptide Enhanced Affinity Receptor (SPEAR™) T-cell platform, has announced that its T-cell therapy has gained access to the European Medicines Agency (EMA)'s Priority Medicines (PRIME) support, for the treatment of some forms of metastatic synovial sarcoma.

Adaptimmune's NY-ESO T-cell therapy targets the NY-ESO cancer antigen present in solid tumors and in hematologic cancer types, including synovial sarcoma and multiple myeloma and has demonstrated signs of efficacy and tolerability in Phase 1/2 trials.

PRIME, so far has accepted 8 drugs while rejecting almost 30, is a new EMA initiative to provide enhanced scientific guidance and support accelerated review of novel investigational therapies that target an unmet medical need. PRIME status is limited to HLA-A0201, HLA-A0205, or HLA-A0206 allele positive patients with inoperable or metastatic synovial sarcoma who have received prior chemotherapy and whose tumor expresses the NY-ESO-1 tumor antigen.

The NY-ESO SPEAR T-cell therapy has recently been designated as orphan medicinal product by the European Commission for the treatment of soft tissue sarcoma. It has also received orphan drug designation and Breakthrough Therapy designation from the US Food and Drug Administration (FDA).

Dr. Rafael Amado, Adaptimmune's Chief Medical Officer commented: "Access to the PRIME initiative represents an important regulatory opportunity for us. It can provide early engagement on the development program with potential for accelerated assessment of data to companies like Adaptimmune who are developing new treatment modalities for patients in Europe with few or no treatment options. Our NY-ESO SPEAR T-cell therapy may help to address the significant unmet medical need of metastatic synovial sarcoma. We look forward to working closely with the EMA throughout its clinical evaluation."

EXPERT PICK

ADAPTIMMUNE GETS KEY REGULATORY DESIGNATION FROM EMA

Adaptimmune was successful in getting itself a spot on the EMA's list of technologies that will have priority medicine (PRIME) status. The designation, analogous to a Fast Track designation in the USA, gives companies developing technologies that address significant unmet needs special regulatory support and expedited review. Adaptimmune received PRIME status for its TCR product in the treatment of inoperable or metastatic synovial sarcoma in patients that are allele-positive for specific HLA molecules and express the NY-ESO-1 antigen. To date, only about 25% of therapies entered for PRIME status have been successful in receiving the designation. Including Adaptimmune's TCR product, fewer than 10 drug products have the status. - *Mark Curtis*

LYSOGENE INITIATES OBSERVATIONAL STUDY OF SANFILIPPO A

Lysogene, a clinical-stage biotechnology company specialized in the development of adeno-associated virus (AAV)-mediated gene therapy for CNS disorders, has announced the initiation of its Sanfilippo A (also known as mucopolysaccharidosis type III or MPS III) multi-national observational study (SAMOS). This prospective natural history study aims to collect information regarding optimal trial design, disease progression and better predictions of future therapeutic effects. Experimental drugs will not be given in the current trial set up, instead, the patients will receive study-related care. Lysogene has enrolled the first patient for the trial and the recruitment is planned before the start of Lysogene's gene therapy (LYSSAF302) trial.

The most common of the four types, Sanfilippo A affects around 100 children in the UK, or one in 89,000 births, and is caused by a lack of the SGSH enzyme, which helps to break down and recycle long-chain sugars. Lack of SGSH results in a build-up of sugars in the body and particularly the brain. Lysogene's next-generation formulation, LYSSAF302, has the potential to replace the defective gene in the cells of Sanfilippo Type A patients and thus prevent neurological damage. Individuals included in the observational study will have the opportunity to enroll in subsequent trials provided they satisfy the enrollment criteria.

Dr. Soraya Bekkali, Lysogene's CMO commented: "This study is critical for comparability of clinical endpoints with the future gene therapy trial and will complement existing published data."

JUNO RESUMES CAR-T TRIAL AFTER ITS CLINICAL HOLD BY THE FDA

Juno Therapeutics, a Seattle-based biopharmaceutical company specialized in the development of cell-based cancer immunotherapies, announced that the FDA removed the clinical hold of its phase 2 ROCKET trial, designed to evaluate the safety and efficacy of CAR-T cells for the treatment of relapsed or refractory B-cell Acute Lymphoblastic Leukemia (ALL). Earlier in July, Juno had halted its CAR-T trial following 3 patient deaths. All the deaths occurred in young patients and were due to cerebral edema.

Juno's Phase 2 ROCKET trial is designed as a single-arm, multicenter study to evaluate the safety and efficacy of JCAR015 for the treatment of relapsed or refractory B-cell ALL (B-ALL). JCAR015, the investigational product, uses genetically modified patient's own T cells to eliminate leukemia cells. The infused T cells express a chimeric antigen receptor (CAR) that has the ability to bind leukemia

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cells that express the CD19 protein on the cell surface and initiate a cell-killing response against the cancer cell.

Patients receiving CAR-T therapies receive doses of chemotherapy beforehand to make the tumor more vulnerable to the CAR-T cells. In the original procedure, Juno used the chemotherapy agent fludarabine and they stated that the deaths are likely attributable to this agent.

The FDA has now agreed for the trial to be continued using cyclophosphamide as the pre-conditioning agent instead of fludarabine. Juno is currently preparing the following four documents for submission to the FDA before it restarts the trial: a revised informed consent form from the patients, a revised investigator brochure, a revised trial protocol and a copy of the presentation to the agency.

Following the news of its clinical hold, Juno's share value had fallen by nearly 30%, while rival Kite Pharma dropped by over 10%. However, the positive news has resulted in an increase in Juno's share by about 25% in after-hours trading.

AVEXIS'S GENE THERAPY CANDIDATE RECEIVES BREAKTHROUGH THERAPY DESIGNATION FROM FDA

AveXis, a clinical-stage gene therapy company specializingin the development of treatments for orphan and life-threatening neurological diseases, has announced that the US FDA has granted Breakthrough Therapy Designation for its gene therapy candidate, AVXS-101, for the treatment of spinal muscular atrophy (SMA).

AVXS-101 is a gene therapy candidate developed for the one-time treatment of SMA type 1 and is the only gene therapy in development for this disease. SMA is a severe neuromuscular disease characterized by the loss of motor neurons leading to progressive muscle weakness and paralysis. It results from a genetic defect in the SMN1 gene which codes for the survival motor neuron (SMN) protein, and affects all muscles in the body. AVXS-101 is designed to address the monogenetic root cause of SMA and prevent further muscle degeneration by addressing the defective and/or loss of the primary SMN gene. Following the announcement, the company's share price increased by 13%.
The present Breakthrough Therapy Designation is based on preliminary clinical results from the ongoing phase 1 trial of AVXS-101, conducted in collaboration with The Research Institute at Nationwide Children's Hospital and The Ohio State University. The FDA's Breakthrough Therapy designation is a process designed to accelerate the development and review of drugs that are intended to treat a serious condition.

The trial is designed as an open-label, dose escalation study to determine the safety and efficacy of gene transfer in SMA type 1 patients. The procedure involves intravenous injection of AVXS-101 through a peripheral limb vein and short-term safety will be evaluated over a period of 2 years. Patients will

be tested at baseline and return for follow up visits on days 7, 14, 21, 30, followed by once every month through 12 months' post dose, and then every 3 months through 2 years post infusion. The trial is expected to complete in December 2017.

Sean P. Nolan, president and CEO of AveXis commented: "We are encouraged to have received Breakthrough Therapy Designation for AVXS-101, and look forward to collaborating with the FDA to determine next steps in the development pathway for AVXS-101. By this action the FDA recognizes the high unmet need for effective treatment options for patients suffering from SMA."

AveXis has been granted Breakthrough Therapy Designation from the FDA for its AAV9-based gene therapy candidate AVXS-001, for the treatment of spinal muscular atrophy (SMA). The designation is based on preliminary clinical results from a phase 1, open-label, dose escalation study in patients with SMA type 1, the most severe form of the condition. Given as a single intravenous administration, the treatment crosses the blood-brain barrier and targets motor neurons to deliver the human SMN transgene. This is a very encouraging development in what is a devastating disease; 90% of SMA type 1 patients will not survive past the age of 2 years. AveXis reported favorable trends in requirements for nutritional and respiratory support at the recent ASGCT meeting which have clearly convinced the FDA of the potential value of this new treatment. – ***Richard Philipson***

CELL THERAPY FOR SPINAL CORD INJURY: UPDATE ON ASTERIAS PHASE 1/2A TRIAL

Asterias Biotherapeutics, a US-based clinical-stage biotechnology company, has announced the completion of enrolment and dosing of a second cohort of 5 patients in its SCiSTAR study. This Phase 1/2a clinical trial is designed to evaluate the activity of escalating doses of AST-OPC1 (oligodendrocyte progenitor cells) in newly injured patients with sensory and motor complete cervical spinal cord injury.

In this cohort, five patients were each administered 10 million AST-OPC1 cells. This represents the first cohort in which patients have been administered a dose high enough to fall within the potentially efficacious range predicted from extensive preclinical studies. The company expects to update safety and efficacy data of this cohort in January 2017.

The SCiSTAR study is partly funded by a $14.3 million grant from the California Institute of Regenerative Medicine. AST-OPC1 is derived from human embryonic stem cells and in vitro and preclinical studies have shown its efficacy in improving the pathologies associated with spinal cord injury.

In addition, Asterias has also provided an update on the observations from the first cohort of 3 patients who received a lower safety dose of AST-OPC1 (2 million cells). All the 3 patients have

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completed their 6-month follow up visit with no serious or unexpected adverse events reported. Interestingly, the patients have shown improvement in their motor function. The company will compare the degree of motor function improvement between the low dose safety cohort and the 10 million cell efficacy cohort to evaluate the dose-response of AST-OPC1.

Asterias had recently received approval from the FDA to expand enrollment in the study, including up to 3 additional patients into this 10 million cell cohort for a total of 8 patients.

Dr. Edward Wirth III, CMO of Asterias commented: "We are now looking forward to initiating enrollment in the high dose 20 million cell efficacy cohort following DMC review of the initial safety data from the current 10 million cell efficacy cohort. In parallel, we will also be expanding enrollment of the study to patients with sensory incomplete injuries, which are less severe than those included in the study so far, under the previously announced FDA-cleared expansion of the ongoing AST-OPC1 study. Enrollment and dosing of this 10 million cell efficacy cohort is also quite significant for Asterias since it paves the way for our very first efficacy readout in January 2017."

CURRENT STATUS OF REGENXBIO'S GENE THERAPY PROGRAMS

REGENXBIO, a US-based biotechnology company specialized in the development, commercialization and licensing of recombinant AAV gene therapy based on its NAV® Technology Platform, has provided an update on four of its lead gene therapy development programs.

Metabolic disease program:

RGX-501 for homozygous familial hypercholesterolemia (HoFH): in collaboration with its development partner, the University of Pennsylvania (UPenn), REGENXBIO is recruiting and screening participants for its Phase I/II clinical trial of RGX-501, for the treatment of HoFH. The company expects to enroll the first patients in the second half of 2016. This Phase I/II clinical trial is designed as an open-label, dose escalation, single-center study to evaluate the safety and efficacy of RGX-501 in up to 12 patients with HoFH.

Neurodegenerative disease programs:

RGX-111 for mucopolysaccharidosis Type I (MPS I) Preclinical Study: The company hopes to submit IND application for a Phase I/II clinical trial in the USA and Canada, in the first half of 2017. RGX-111 uses the AAV9 vector to deliver the human α-l-iduronidase (IDUA) gene to the CNS. RGX-121 for mucopolysaccharidosis Type II (MPS II) Preclinical Study: The company will initiate the production of RGX-121 in the fourth quarter of 2016 to support its planned Phase I/II clinical trial. RGX-121 uses the AAV9 vector to deliver the human iduronate-2-sulfatase (IDS) gene to the CNS.

Retinal disease program:

RGX-314 for wet age-related macular degeneration (wet AMD) Preclinical study: REGENXBIO

is currently conducting additional preclinical studies on RGX-314, for the treatment of wet AMD, as recommended by the FDA's Center for Drug Evaluation and Research during a pre-IND meeting in April 2016. RGX-314 uses an AAV8 vector to deliver a gene for a monoclonal antibody fragment that binds to anti-vascular endothelial growth factor and neutralizes VEGF activity.

Kenneth T. Mills, President and CEO of REGENXBIO commented: "The development and clinical operations teams at REGENXBIO and the University of Pennsylvania are working to ensure that our first-in-human gene therapy clinical trials are well-designed and enroll the patients most likely to benefit from treatment, which supports our long-term clinical development plans and our mission of improving the lives of patients suffering from severe diseases. We look forward to dosing the first patients in the RGX-501 clinical trial in the coming months and expect to have active INDs for our four lead programs in 2017."

FDA GRANTS FAST TRACK DESIGNATION FOR CALADRIUS' CLBS03

Caladrius Biosciences, a New York-based cell therapy manufacturing company, has announced that its product candidate CLBS03 (autologous expanded polyclonal regulatory T cells) has received Fast Track designation from the FDA, for the treatment of recent-onset type 1 diabetes (T1D). T1D with residual beta cell function is recognized by the FDA as an orphan disease.

The trial is designed as a randomized, placebo-controlled, double-blind Phase 2 clinical study to evaluate the safety and efficacy of CLBS03 administration as a treatment for T1D. The study is being conducted in collaboration with Sanford Research, a subsidiary of Sanford Health. Subjects will be randomized into one of three groups and will receive either a high dose of CLBS03, a low dose of CLBS03 or placebo. The key endpoints of the trial include measurement of pancreatic beta cell function, glucose and hemoglobin A1c levels and preservation of C-peptide.

Dr. David J. Mazzo, CEO of Caladrius commented: "Obtaining Fast Track designation is a key milestone in our regulatory and development strategy for CLBS03. It underscores the great need for innovative treatments, such as CLBS03, in the treatment of T1D and allows for the acceleration of its development," said "We are making excellent progress advancing the U.S.-based Phase 2 clinical program of CLBS03 to treat T1D and look to complete enrollment of the first cohort of 18 patients in the coming weeks. This, coupled with our Orphan Drug and Fast Track designations, should make CLBS03 an even more attractive opportunity for a potential partner."

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CHINA TO START THE FIRST PHASE 1 CRISPR CLINICAL TRIAL

A team of Chinese scientists led by Prof. Lu You of Sichuan University, have obtained approval from the university hospital's ethics board, to initiate a Phase 1 clinical trial using the CRISPR-Cas9 gene editing technology. China has again stolen the limelight in becoming the pioneers to start the first CRISPR clinical trial, following their headstart in using CRISPR to edithuman embryos, as well as monkeys.

CRISPRtechnology has rapidly changed the face of biological research, such that precise genome editing has now become a reality within years of its initial development. CRISPR-Cas9 gene editing technology has been applied to many aspects of cancer research, including research on tumor genes, constructing animal tumor models and cancer gene therapy.

In the CRISPR procedure, researchers will extract T cells from blood of the patients with lung cancer and perform CRISPR editing. This edit will remove the gene for a protein, PD-1 (programmed cell death protein 1) that identifies the T cells as immune cells and prevent the cancer cells from disabling them. Researchers will select and expand these edited cells *ex vivo* and then infuse them back into the patient. A single dose of cyclophosphamide at 20 mg/kg will be administered 3 days before cell infusion. IL-2 will also be given in the following 5 days, with patients getting a total of two, three or four cycles of treatment.

This first clinical trial is designed to test whether CRISPR is safe for use in people, rather than whether it effectively treats cancer or not. It will examine the effects of three different dosage regimens on 10 patients. The study will be conducted at the West China Hospital (Sichuan University) and is expected to complete in 2018. Chengdu MedGenCell, a biotechnology company and a collaborator on the trial, will validate the cells to ensure that the correct genes are knocked out before the cells are re-introduced into the patients.

In June, we had reported the approval of a US CRISPR clinical trial by the National Institute of Health (NIH). That trial planned by the University of Pennsylvania was expected to be the first CRISPR trial in patients; however, it is still awaiting approval by the FDA and the individual medical centers.

ZIOPHARM PLANS PHASE 1 CLINICAL TRIAL WITH CD33 CAR-T CELLS

Ziopharm Oncologyhas announced its plans for a Phase 1 adoptive cell therapy clinical trial using CAR-T cell technology, to treat patients with relapsed or refractory acute myeloid leukemia (AML).

The company, in collaboration with Intrexon Corporation and the

MD Anderson Cancer Center, will conduct the trial utilizing autologous T cells transduced with lentivirus to express a CD33-specific CAR. The basis for this clinical trial originates from positive preliminary results from *in vivo* and pre-clinical studies, which have demonstrated that lentiviral-mediated transduction of CAR-T cells targeting CD33 exhibit specific cytotoxic activity for CD33+ AML cells and enhance survival of AML mouse models.

Dr. Laurence Cooper, Ziopharm's CEO commented: "As we progress through the remainder of 2016 with our Intrexon Corporation and MD Anderson collaborators, we believe that our CD33 CAR-T cell approach has the potential to positively impact a disease area that has been largely unexplored with this type of immune-therapy and overall this malignancy has seen inadequate improvement in treatment options. We look forward to moving into the clinic as soon as possible to help patients with advanced AML urgently in need of new therapies."

CELYAD PARTNERS WITH ONO TO DEVELOP T-CELL IMMUNOTHERAPY

Celyad a company specialized in the development of engineered cell therapies, has entered into an exclusive license agreement with Japanese immuno-oncology company, ONO Pharmaceutical. This collaboration aims to further the development and commercialization of Celyad's allogeneic NKR-2 T-cell immunotherapy in Japan, Korea and Taiwan. Celyad has also granted to ONO, an exclusive option to license its autologous NKR-2 T cell product in the above ONO territories.

Under the terms of the agreement, ONO will pay Celyad an upfront payment of $12.5 million and Celyad is eligible to receive up to $299 million in development and commercial milestones. Celyad will also receive double digit royalties on net sales in ONO territories.

Celyad will continue developing its allogeneic NKR-2 T-cell immunotherapy in the EU and US territories, and ONO will be responsible for future development and commercialization in ONO's territories (Japan, Korea and Taiwan).

Dr. Christian Homsy, CEO of Celyad commented: "We are very pleased to collaborate with ONO and to activate the development of our NKR-2 T-cell allogeneic platform in Japan, Korea and Taiwan. This license agreement is a great opportunity for Celyad to expand the scope of its immuno-oncology clinical programs and bring this breakthrough science to numerous patients around the world. Further, this license agreement with ONO, the leader in immuno-oncology in Asia, validates our NKR-2 approach and its tremendous potential."

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APTUIT LLC & DIMENSION THERAPEUTICS COLLABORATE TO ADVANCE GENE THERAPY PROGRAMS

Aptuit LLC, a drug discovery and development contract research organization (CRO), has entered into a strategic partnership agreement with Dimension Therapeutics for the development of Dimension's AAV-mediated gene therapy programs.

Dimension Therapeutics is a biopharmaceutical company specialized in developing liver-directed gene therapy treatments for severe and rare genetic disorders. Dimension's lead gene therapy programs include treatments for hemophilia A and B, ornithine transcarbamylase deficiency and glycogen storage disease type Ia. Aptuit LLC is contributing its IND-enabling good laboratory practice (GLP) studies for select rare disease programs at Dimension. Three key integrated development projects have initiated under the partnership.

Jonathan Goldman, CEO of Aptuit LLC commented: "This partnership is designed to accelerate select late preclinical-stage programs at Dimension in a high-quality environment, supported by a culture of scientific excellence and innovation. This best-in-class partnership builds upon Aptuit's scientific excellence in integrated IND development in the exciting area of gene therapies. In particular, we plan to ensure full and timeline resourcing of these programs, in order to increase probability of success, and reduce time and cost."

GE HEALTHCARE ACQUIRES BIOSAFE FOR THE DEVELOPMENT OF LIFE-SAVING CELLULAR THERAPIES

As part of GE Healthcare's strategy to develop a digitally-enabled ecosystem of tools, solutions and services for cell therapy, it has acquired Biosafe Group, a Switzerland-based supplier of integrated cell bioprocessing systems. The acquisition expands GE's technology reach to a number of new cell therapy types.

Kieran Murphy, CEO Life Sciences, GE Healthcare commented: "GE is building a world-class set of tools, technologies and services for cell and gene therapy and Biosafe's expertise and innovative systems will strongly enhance our customer offering. GE and Biosafe share a vision of an integrated approach to helping customers optimize every stage of their process to reduce production risks dramatically and increase access to these remarkable new medicines.

Currently, GE is partnering with experts in the industry, such as Canada's Centre for the Commercialization of Regenerative Medicine, the UK's Cell and Gene Therapy Catapult, Australia's Cell Therapy Manufacturing Cooperative Research

Centre and leading clinical centers such as UPenn, Karolinska Institute, Memorial Sloan-Kettering and Mayo Clinic.

Claude Fell, Founder and Chairman, Biosafe Group commented: "Together with GE we will have the combination of biological, engineering and industrial capabilities to help accelerate the fields of cell therapy and cellular immunotherapy into the mainstream, benefitting patients globally, and bringing the vision of personalized medicine to reality."

EVOTEC ENTERS AGREEMENT WITH MIT AND HARVARD

Evotec, a Germany-based service provider for drug discovery solutions, has entered into a non-exclusive license agreement with the Broad institute of MIT and Harvard for the use of CRISPR-Cas9 gene editing platform.

Under the terms of the agreement, Evotec has gained access to the intellectual property rights related to CRISPR-Cas9 technology and will use this to expand its drug discovery portfolio. Evotec has long-term discovery alliances with partners including Bayer, Genentech, Janssen Pharmaceuticals, AstraZeneca and Roche.

CELL MEDICA ACQUIRES DELENEX TO EXPAND ITS CELL THERAPY PORTFOLIO

Cell Medica, a London-based pharmaceutical company specialized in the development of cellular therapeutics for the treatment of cancer and infectious diseases, has acquired Swiss-based Delenex Therapeutics. Delenex is a clinical-stage biopharmaceutical company focused on the development of locally and systemically applied antibody therapeutics. The acquisition will combine Cell Medica's expertise in creating chimeric antigen receptors (CAR) with Delenex's proprietary PENTRA® technology, to create next generation CAR-modified cellular immunotherapies with improved functionality and specificity. The financial details of the acquisition were not disclosed.

In June, Cell Medica signed a co-development partnership and exclusive licensing agreement with Baylor College of Medicine, to create next-generation cellular immunotherapy products for the treatment of cancer.

Gregg Sando, CEO of Cell Medica commented: "The acquisition of Delenex provides a key enabling technology for the development of an exciting pipeline of next generation CAR-modified cell therapies. We are delighted to welcome the talented team from Delenex and to join the vibrant Swiss biotech community based in Schlieren."

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EDITAS SIGNS COLLABORATIVE AGREEMENT WITH SAN RAFFAELE TIGET

Editas Medicine, Inc. and Fondazione Telethon and Ospedale San Raffaele, which operate a joint research collaboration known as the San Raffaele Telethon Institute for Gene Therapy (SR-TIGET), have entered into a scientific collaboration to research and develop genome edited hematopoietic stem cell (HSC) and T cell therapies.

The scientific work at SR-TIGET in Milan, Italy will be led by Prof. Luigi Naldini, SR-TIGET Director and a world-renowned expert in lentiviral gene therapy and hematology. The goal of the 3-year research collaboration includes the development of gene correction strategies for the treatment of rare diseases, including two specified indications in the blood and bone marrow. This collaboration is part of Editas Medicine's overall HSC and T cell editing product development strategy for challenging disease areas.

The San Raffaele Institute for Gene Therapy (SR-TIGET) has again shown its desire to forge links with industry through its collaborative agreement with Editas Medicine Inc. The Italian institute, which is the result of joint collaboration between Fondazione Telethon and Ospedale San Raffaele, already has collaborative agreements with GSK (which led to the recent approval of the γ-retroviral therapy STRIMVELIS for ADA-SCID) and Biogen Idec (to develop lentiviral gene therapies for hemophila A and B). The new agreement with Editas is sketchy in its scope and disease targets – "the development of gene correction strategies for the treatment of rare diseases, including two specified indications in the blood and bone marrow" – but promises to increase further the competition in gene editing technologies and places SR-TIGET at the forefront of the field. – *Richard Philipson*

BIOLIFE ENTERS 10-YEAR SUPPLY AGREEMENT WITH KITE PHARMA

BioLife Solutions, a Washington-based provider of biopreservation tools for cells, tissues and organs has announced that it has entered into a 10-year supply agreement with Kite Pharma, for Kite's CAR T cell therapy.

The agreement will provide Kite with BioLife's CryoStor clinical grade freeze media for cells and tissues, for the manufacturing process of KTE-C19, a CAR T cell therapy currently in four clinical trials for various cancers. KTE-C19 is an investigational therapy in which a patient's T-cells are genetically modified to express a CAR designed to target the antigen CD19, a protein expressed on the cell surface of B-cell lymphomas and leukemias.

KITE ENTER LICENSE AGREEMENTS WITH UCLA & NIH

Kite Pharma, a clinical-stage biopharmaceutical company, has announced that it has entered into an exclusive, global license agreement with the University of California, Los Angeles (UCLA), to advance the development of off-the-shelf allogeneic T-cell therapies from renewable pluripotent stem cells.

The technology is based on research developed in the laboratory of Prof. Gay M. Crooks at UCLA. The group developed an artificial thymic organoid (ATO) cell culture system that mimics the human thymic environment to support efficient *ex vivo* differentiation of T-cells from primary and reprogrammed pluripotent stem cells.

Under the terms of this agreement, Kite will receive exclusive rights to use the licensed technology to develop and commercialize T-cell products in oncology. In connection with the license agreement, Kite has entered into a sponsored research agreement with UCLA to support ongoing preclinical research in Dr. Crooks' laboratory to optimize the ATO platform.

In a move to expand its CAR-T therapy portfolio, Kite has also entered into an exclusive worldwide license agreement with the NIH for intellectual property related to human anti-CD19 CAR-based products desgined for the treatment of B-cell malignancies. The National Cancer Institute (NCI) is currently conducting a Phase 1 clinical trial of the product candidate in patients with B-cell malignancies under an existing Cooperative Research and Development Agreement between Kite and the NCI.

ONES TO WATCH

KITE TO GO AFTER PLURIPOTENT-DERIVED OFF-THE-SHELF T CELLS

Both Cellectis and Adaptimmune have differentiated themselves with development programs to produce universal T cells, which can be bulk manufactured and deployed in an allogeneic setting for cancer treatment. Kite Pharma announced this past month that it too will pursue a universal T cell approach, with one key difference – rather than using donor T cells like Cellectis and Adaptimmune, they will produce T cells from both primary and reprogrammed stem cells (PSCs). The goal of PSCs as a source is to improve yields and circumvent barriers imposed by donor-to-donor variability. Kite in-licensed the cell culture technology from UCLA, which mimics *in vivo* development of T cells using artificial thymic organoids. Co-culture approaches do present commercialization challenges when it comes to manufacturing and cost, but the proof will be in the pudding, and if Kite can make this commercially viable it would be a significant advance for the field. – *Mark Curtis*

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GENSIGHT RAISES 40 MILLION EUROS IN IPO

GenSight Biologics, a Paris-based clinical-stage biotechnology company specialized in developing gene therapies for retinal diseases such as Leber Hereditary Optic Neuropathy (LHON), has raised 40 million euros in an initial public offering.

The funds will provide support for GenSight's various gene therapy clinical trials for vision loss in LHON. Last month, GenSight announced promising results from its Phase I/II gene therapy trial designed to treat LHON.

TRAKCEL APPOINTS RAVI NALLIAH AS CEO

TrakCel, a Cardiff-based service provider specialized in providing digital traceability technology to the cell therapy industry, has announced the appointment of **Ravi Nalliah** as its CEO This move is part of TrakCel's strategic plan to expand leadership in line with its clinical and commercial growth. Mr Nalliah succeeds Keren Winmill, who will continue as TrakCel's Board Chairman.

Mr Nalliah joins TrakCel from PCI Services, a US-headquartered service provider for the drug development industry, where he was the Chief Finance and Strategy Officer of the business and its subsidiaries.

CALIMMUNE EXPANDS ITS LEADERSHIP TEAM

Calimmune, a US-based clinical-stage gene therapy company specialized in genome editing, has appointed **Dr. Jeffrey Bartlett** as its new CSO and Tana Session as Vice President of Human Resources.

Dr. Bartlett has more than 20 years of experience in cell and gene therapies. Most recently, he served as vice president of research and development at Calimmune. Prior to that, Dr. Bartlett held various scientific positions at the Nationwide children's hospital, Ohio state university and the University of North Carolina at Chapel Hill. He was also the scientific founder of Nexigen Biologics and served as an advisory committee panel member for the National Institute of Health and FDA.

Before joining Calimmune, Ms Session served in several executive positions in human resources for diverse New York- and California-based public and private institutions, including The Center for Discovery, and Coleman Research Group.