

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: Two important milestones have been achieved this month: GlaxoSmithKline (GSK) has agreed a price with the Italian Medicines Agency (AIFA) for Strimvelis, its *ex vivo* γ -retroviral gene therapy treatment for the hereditary immunodeficiency syndrome ADA-SCID; and Spark Therapeutics has released positive long-term follow-up clinical data from its adeno-associated virus-mediated gene therapy program in Leber's congenital amaurosis type 2, a blinding disease caused by deficiency of the *RPE65* gene in the retinal pigment epithelium. The news on GSK's product is particularly interesting, because a 'price-for-performance' approach has been agreed, although the details of what will constitute a successful clinical outcome for the treatment are not described. Even if the full agreed price for the one-off treatment of \$665,000 is paid, this will almost certainly not provide GSK with a commercial return for the treatment.



GENE THERAPY
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CELL THERAPY
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CELL THERAPY: Lion Biotechnologies continues to be the sole industry champion of tumor infiltrating lymphocytes (TILs), a subset of T cells that are naturally inclined to penetrate solid tumors and eradicate cancer cells. The



company extended its Cooperative Research and Development Agreement (CRADA) with the National Cancer Institute (NCI) for an additional 5 years, through to 2021, to continue the investigation of unmodified TILs in treating cancer under the supervision of Steven Rosenberg. TILs present a number of translational complexities, including a high degree of heterogeneity, even with the same tumor, which has made their characterization challenging. A dose of TIL is also labor intensive to produce, requiring mechanical dissociation of a tumor sample, enzymatic digestion into a single cell suspension and significant scale-up. Lion Biotechnologies has a number of exclusive, global licenses from the NCI to develop TILs for a number of indications, including melanoma, breast, bladder, lung and HPV-associated cancers. While there will be manufacturing challenges to come, the company has more than \$190 million on its balance sheet to deploy for the development work.



WORLD'S FIRST PEDIATRIC GENE THERAPY OFFERS A MONEY-BACK GUARANTEE

GSK's Strimvelis, an *ex vivo* stem cell gene therapy for adenosine deaminase deficiency with severe combined immunodeficiency (ADA-SCID), will be offered for sale in Europe with a money-back guarantee. Priced at €594,000 (\$665,000), it's among the most expensive therapies in the world.

AIFA, the national authority responsible for drug regulation in Italy, has set the price and terms during negotiations with GSK for the sale of Strimvelis in Europe. Professor Luca Pani, Director General of AIFA commented: "The drug has to deliver what you say or we don't pay. If it does not work, they will return the money."

ADA is a rare, autosomal recessive metabolic disease characterized by SCID. Due to the weak immune system with which the babies are born, the disease is sometimes referred to as 'bubble baby' disease. It occurs in fewer than 1 in 100,000 live births worldwide.

Strimvelis was developed by GSK and the Italian firms Fondazione Telethon and Ospedale San Raffaele. GSK received EU approval for Strimvelis following a positive opinion from the European Medicines Agency earlier this year. The data supporting this gene therapy was collected from 18 children with ADA-SCID. Patients were treated with an autologous CD34+ enriched cell fraction that contained CD34+ cells transduced with a retroviral vector encoding the human ADA cDNA. Except 3, all the remaining children were cured of ADA-SCID and are alive today.

According to the MIT Technology review, GSK will only offer the treatment in Milan, requiring patients to travel there for availing the treatment. Professor Pani has confirmed that the Italian price will apply to all of Europe. Patients receiving GSK's gene therapy will be tracked in AIFA's registry, which has already

imposed pay-for-performance rules on some cancer drugs. AIFA maintains 135 patient registries to track

how well they work and according to Professor Pani, Italy has collected more than €250 million in refunds.



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

Asterias Biotherapeutics, a US-based clinical-stage biotechnology company, has received safety clearance from its Data Monitoring Committee to pursue dosing of a third cohort of subjects in its SCiSTAR study. This ongoing 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. The safety data was obtained from an initial cohort of three patients who received 2 million AST-OPC1 cells and a second cohort of five patients who were dosed with 10 million AST-OPC1 cells. No serious or unexpected adverse events related to AST-OPC1 administration were observed in any of the two cohorts of patients. The third cohort of 5–8 patients will be administered with the highest dose of 20 million cells.

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, the study is also proceeding with enrolling the first cohort of 5–8 sensory incomplete cervical spinal cord injury patients, each of whom will be dosed with 10 million cells.

Dr Edward Wirth III, CMO of Asterias commented: “The positive safety data in the previous Phase 1 study and in the ongoing Phase 1/2a study gives us the confidence to now proceed to administration of 20 million cells, which based on our significant preclinical research is likely well within the dosing range where we could expect to see clinically meaningful improvement in these patients.”



EXPERT PICK

ASTERIAS MOVES TO HIGH DOSE IN SPINAL CORD INJURY

California-based Asterias Therapeutics has been given a green light by its Data Monitoring Committee to begin dosing patients with 20 million cells in its ongoing Phase 1/2a study investigating human embryonic stem cell-derived oligodendrocyte progenitors in patients with complete spinal cord injury. The first two cohorts of patients received 2 and 5 million cells per dose. So far, no adverse events have resulted from the administration of AST-OPC1, suggesting the PSC-derived therapy is safe. The larger question that looms is efficacy. Initial readouts from the cohort that received 10 million cells are anticipated in January 2017. – Mark Curtis



CARIBOU DEVELOPS NEW METHOD TO PROFILE CRISPR-CAS9 GENE EDITING OUTCOMES

Caribou Biosciences, a California-based pharmaceutical company specialized in the development of CRISPR-Cas technologies, has announced a new discovery by its scientific team that predicts the DNA repair outcomes following Cas9 cleavage of DNA. This discovery of the ability to control DNA repair outcomes has significant implications for the use of CRISPR-Cas9 in product development.

Despite the widespread use of CRISPR-Cas9 technology to induce double-strand breaks (DSBs) for genome engineering, the resulting repair products have not yet been studied fully. In the study published in *Molecular Cell*, a team of Caribou researchers led by Dr Andrew May spliced 223 sites in the human genome with Cas9 and analyzed the DNA repair profiles at each site. They discovered that the DNA repair is non-random and generates reproducible patterns at each target site. The study also demonstrated that the repair outcomes are determined by the protospacer sequence rather than

genomic context, indicating that DNA repair profiling in cell lines could be used to predict repair outcomes in primary cells. It also demonstrated how these non-random outcomes could be harnessed to produce a desired effect, such as a gene knockout or the reading frame restoration of a disease-causing allele. Taken together, the research elucidates a strategy for using error-prone DNA-repair machinery to generate precise edits.

Dr May, CSO of Caribou, commented: “This discovery represents a fundamental advance in the development of CRISPR-Cas9 technology. Through careful measurement of the outcomes of the DNA repair machinery, we can understand the specific patterns of editing that occur within a cell population with a high degree of certainty. Caribou is at the forefront of cutting-edge research in genome engineering, and I am delighted that our world class scientific team continues to make significant contributions to develop the potential of CRISPR-Cas9 gene editing technology.”



LION RECEIVES A 5-YEAR EXTENSION OF CRADA FOR DEVELOPMENT OF CANCER IMMUNOTHERAPIES

Lion Biotechnologies, a clinical-stage biopharmaceutical company specialized in the development of TIL-based cancer immunotherapies, has announced the amendment of its CRADA with the NCI

to extend the agreement for an additional 5 years, until 2021.

Lion entered into CRADA in 2011 for the development of TIL therapy in the treatment of metastatic melanoma. This agreement

was later amended in 2015, to increase its annual funding and to include four additional indications—bladder, lung, breast and HPV-associated cancers. The current amendment aims to investigate the potential of combining TIL with FDA-approved drugs such as checkpoint inhibitors, for the treatment of the five indications covered under CRADA. No changes were made to the financial terms and investigation team.

Dr Maria Fardis, president and CEO of Lion Biotechnologies, commented: “We continue to explore the potential utility of the TIL technology in treating multiple solid tumor indications in our commitment to offer TIL to patients. The amendment to the CRADA provides for further investigation of TIL in multiple indications as single regimen as well as in combination with other FDA-approved therapies, such as checkpoint inhibitors.”



SPARK'S GENE THERAPY TRIAL FOR RETINAL DISEASES SHOWS POSITIVE OUTCOME

Spark Therapeutics, a US-based gene therapy company, has announced new positive data from its Phase 3 trial of Voretigene Neparvovec, for the treatment of inherited retinal diseases caused by mutations in the *RPE65* gene.

Spark's voretigene neparvovec (formerly referred to as SPK-RPE65) employs an adeno-associated virus-mediated gene therapy to restore, halt or slow the decline of patient's vision caused by mutations in *RPE65*. It has received both breakthrough therapy and orphan product designations from the US Food and Drug Administration (FDA), as well as orphan product designation from the European Medicines Agency.

The present Phase 3 trial of voretigene neparvovec is a randomized controlled, multicenter trial conducted in 31 subjects with confirmed *RPE65* gene mutations. The modified intent-to-treat (mITT) population included 20 subjects in the intervention group and nine in the control group. Voretigene

neparvovec was administered to both the eyes of 20 subjects in the mITT group. After 1 year of undergoing the same retinal and visual function testing as the intervention subjects, all nine subjects in the mITT control group elected to crossover and receive voretigene neparvovec in both eyes.

Data revealed by Spark showed that, of the nine crossover subjects, eight responders demonstrated the maximum improvement measurable on the primary endpoint at 1 year. A total of 27 of 29 subjects demonstrated a gain of function at 1 year. Follow-up data shows the durability of benefit for at least 2 years in the Phase 3 intervention group.

Spark has already released data for its Phase 3 301 trial, which showed statistically and clinically significant improvement in the intervention group compared to the control group on the primary endpoint, change in bilateral mobility testing (MT). The first two secondary endpoints – full-field

light sensitivity threshold testing (FST) for white light and MT for the assigned first eye – also showed significant improvement. But the study did not meet the third secondary endpoint, visual acuity.



EXPERT PICK

Spark Therapeutics continues to blaze a trail for ocular gene therapy treatments. Its lead product, voretigene neparvovec (AAV2-hRPE65v2), has been in clinical development for several years for Leber's congenital amaurosis type 2, and the release of new Phase 3 clinical data adds

to an already impressive data set from the Phase 1 program. The latest clinical data shows an improvement in mobility testing and light sensitivity 1 year after treatment to both eyes, which appears to be durable in a subset of patients who have been followed for 2 years. The company has taken a logical and systematic approach to developing the treatment, first by treating a single eye, then by interval treatment of the second eye (showing no adverse immunological effects) and are now able to present positive data after treatment to both eyes. The company has a rolling BLA to which the new data will be added – an application for approval must be on the horizon now! – Richard Philipson



CARDIOCELL'S PHASE 2A TRIAL USING MSCS OFFER HOPE FOR HEART FAILURE PATIENTS

CardioCell has presented data of its Phase 2a clinical trial at the European Society of Cardiology congress. The trial evaluates the safety and efficacy of intravenous (IV) infusion of ischemia-tolerant allogeneic mesenchymal stem cells (itMSCs) in patients with non-ischemic cardiomyopathy.

CardioCell LLC is a California-based global biotechnology company specialized in the development of stem cell-based therapeutics for cardiovascular indications. It is a subsidiary of Stemedica Cell Technologies and uses its patented, bone marrow-derived, allogeneic, itMSCs to explore its therapeutic potential for various cardiovascular indications, including acute myocardial infarction, chronic heart failure and peripheral artery disease.

Dr Javed Butler, one of the protocol designers of the study,

presented data at the 'Hot Line' session, illustrating statistically significant improvement in 6-minute walk test, quality-of-life scores as assessed by Kansas City Cardiomyopathy Questionnaire (KCCQ) and favorable immune modulatory benefits.

This Phase 2a trial is designed as a single blind, placebo-controlled, crossover, multicenter study to deliver itMSCs via IV infusion to 22 enrolled patients with non-ischemic cardiomyopathy. The progress of the treatment was tracked at the baseline, 90 days and 180 days, and was measured by the KCCQ, 6-minute walk, New York Heart Association (NYHA) score and cardiac MRI. Crossover was performed at 90 days after the first injection, where the control group received CardioCell's treatment, and the original treatment group received the placebo

solution. The study is expected to complete by mid-2017.

Results showed that the IV injection strategy was safe and well tolerated. No major differences in any of the safety endpoints were observed between the control and treatment group. Interestingly, IV itMSC injections exhibited improvements in several clinical-efficacy endpoint measurements, including statistically significant improvement in 6-minute walk test and KCCQ. The study

also demonstrated the potential of itMSCs to suppress inflammation, which was evident by the reduction in natural killer (NK) cells. Data analysis before the 90-day crossover revealed a statistically significant improvement in the left ventricular end systolic and diastolic volumes in the itMSC-treated groups.

The study represents the first clinical trial to study the potential of IV administration of itMSCs in patients with chronic heart failure.



RETROSENSE INITIATES GENE THERAPY TRIAL FOR RETINITIS PIGMENTOSA

RetroSense Therapeutics, a US-based biopharmaceutical company focused on the development of gene therapies for retinal degenerative diseases, has announced the successful completion of its low-dose cohort study for the treatment of retinitis pigmentosa (RP).

RetroSense's Phase 1/2a gene therapy trial is designed as an open-label, dose-escalation study to determine the safety and tolerability of unocular intravitreal injection of RST-001 in patients with RP. Intravitreal administration of RST-001 delivers a photo switch, channelrhodopsin-2, to cells in the retina of the eye. When expressed, the channelrhodopsin-2 protein depolarizes in response to light, thus generating a signal that is transmitted to the brain. RetroSense has announced that the low-dose cohort of patients has been safely dosed in the initial clinical trial to evaluate the safety of RST-001. RetroSense has also confirmed that no inflammation or ocular adverse events were seen in any of these patients.

RST-001 cleared the Investigational New Drug (IND) application from the US FDA in late 2015. The

study is composed of two parts and is aimed to primarily examine the safety of RST-001 administration in patients. An initial dose-ranging study (part 1) will investigate three dose levels of RST-001 in three separate groups of adult patients with advanced RP. This step is aimed to determine a single dose of the experimental agent that is safe and well tolerated to further test in the second part of the study. The second part, which will be conducted in a fourth set of patients, is aimed to obtain additional safety data at the highest tolerated dose and to provide additional clinical data to guide the design of future efficacy studies. The trial, which is currently recruiting patients, is expected to complete by April 2017.

Sean Ainsworth, CEO of RetroSense, commented: "We are quite pleased with the safety profile we have observed in this low-dose cohort of patients. Going into our mid-dose cohort with the strong safety profile we have seen early on suggests potential for a higher therapeutic index – or, potentially better safety and efficacy outcomes – for RST-001."



CELL MEDICA SIGNS AGREEMENT WITH UCL TO ADVANCE TCRs FOR CANCER TREATMENT

Cell Medica, a London-based pharmaceutical company specialized in the development of cellular therapeutics for the treatment of cancer and infectious diseases, has announced a research collaboration agreement with University College London (UCL) to develop engineered T-cell receptor (TCR)-based technologies for the treatment of cancer. The collaboration, which is built on the research works of Professors Hans Stauss and Emma Morris of UCL, will provide Cell Medica with an exclusive license over UCL's TCR technologies, as well as TCR gene sequences for the development and commercialization of specific products.

Under the terms of the agreement, both parties can bring platform technologies to the collaboration, aiming to generate engineered TCR products. The companies have also signed a sponsored research agreement under which Cell Medica will fund all research and development, with an exclusive option

to license all products developed within the collaboration. Cell Medica has paid an up-front fee and will make additional payments for its exclusive option to license future products.

UCL will conduct the preclinical and early clinical research under the guidance of a joint steering committee. Cell Medica will support the product development work with its expertise in manufacturing clinical-grade cell therapies and establishing robust production processes suitable for industrial scale-up.

Gregg Sando, CEO of Cell Medica, commented: "This collaboration adds the modified TCR technology platform to our strategy to develop breakthrough treatments for cancer using cellular immunotherapy products. The partnership with Profs Hans Stauss and Emma Morris, leading researchers in this field, should enable us to generate a pipeline of new TCR products with increased efficacy and safety for patients."



RETROSENSE'S OPTOGENETICS RECEIVES US PATENT

RetroSense Therapeutics has announced that the US Patent and Trademark Office (USPTO) has granted US patent for its proprietary method for restoring vision using optogenetics. RetroSense is the exclusive licensee of this intellectual property and the patent broadly covers methods for

restoring or improving vision using optogenetic approaches. The allowed claims cover the use of various opsins and rhodopsins in restoring vision.

The company is developing its optogenetic-based lead candidate RST-001 for the treatment of RP and advanced dry age-related

macular degeneration and is currently in a Phase 1/2a trial. Intravitreal administration of RST-001 delivers a photo switch, channelrhodopsin-2, to cells in the retina of the eye. When expressed, the channelrhodopsin-2 protein depolarizes in response to light, thus generating a signal that is transmitted to the brain.

Dr Richard H Masland, the inventor of the method, and David G Cogan, Professor of Ophthalmology at Massachusetts Eye and Ear Infirmary, commented: “This is an important milestone in the quest to develop a therapy to restore or improve vision for patients suffering from RP or advanced dry age-related macular degeneration.”



PFIZER ACQUIRES BAMBOO TO EXPAND ITS GENE THERAPY PORTFOLIO

With its latest acquisition of Bamboo Therapeutics, a North Carolina-based pharmaceutical company specialized in gene therapy, Pfizer aims to become a major gene therapy player in the industry.

The acquisition will combine Bamboo's gene therapy expertise in advanced vector design and production technologies with Pfizer's global scale, research, development and commercialization experience. Pfizer had already purchased approximately 22% of the company during the first quarter of 2016 for about \$43 million. It has now purchased the remaining company for an upfront of \$150 million. Following the latest acquisition, Bamboo Therapeutics is now a wholly owned subsidiary of Pfizer.

Bamboo Therapeutics is developing adeno-associated virus (AAV) vector-based gene therapies for central nervous system and neuromuscular disorders. Its portfolio includes pre-clinical assets for Duchenne muscular dystrophy, Friedreich's ataxia and Canavan disease, and a Phase 1 asset for giant axonal neuropathy. In addition to the pipeline, Pfizer also gains Bamboo's gene therapy manufacturing

facility, which has the experience of producing resources for Phase 1/2 trial. The facility, previously known as the University of North Carolina Vector Core facility, has served as a qualified supplier of rAAV vectors for several healthcare companies and academic institutions.

Pfizer's investment in gene therapy began in 2014 when it signed a deal with Spark Therapeutics for hemophilia gene therapy. At the same time, it also started a dedicated gene therapy research center in London, known as the Genetic Medicines Institute. The company also has several ongoing academic research agreements, including one with King's College London to develop a series of rAAV gene therapy vectors and another with the University of Iowa Research Foundation to develop a potential gene therapy for cystic fibrosis. In addition, Pfizer has also entered into collaboration with Emeryville, CA-based Molecular Therapeutics (4DMT) to discover and develop next-generation rAAV vectors for cardiac disease. Acquisition of Bamboo Therapeutics is the last in the list of its expansion strategy to become a major gene therapy player.



BIOCARDIA SIGNS MERGER AGREEMENT WITH TIGER X MEDICAL TO ADVANCE CELL THERAPY

BioCardia, a California-based clinical-stage company specialized in the development of regenerative therapeutics for cardiovascular diseases, has entered into a merger agreement with Tiger X Medical to advance cell therapy for heart diseases.

The merged entity will trade on the over-the-counter markets and will focus on the business of BioCardia. The company will have a combined \$23 million in cash to advance a BioCardia cell therapy system.

BioCardia has two cell-based product candidates in clinical development, CardiAMP and CardiALLO. CardiAMP uses autologous bone marrow-derived cells and CardiALLO uses universal donor mesenchymal stem cells. The CardiAMP

clinical trial is a randomized controlled, multi-center study of 250 patients designed to evaluate the effectiveness of CardiAMP therapy for heart failure. The FDA has approved the study under an Investigational Device Exemption. CardiAMP is also in clinical trial for sub-acute myocardial infarction and CardiALLO is in clinical testing for heart failure.

Dr Peter Altman, CEO of BioCardia, commented: “Our CardiAMP cell therapy is seeking to address an enormous unmet need – a treatment for heart failure that develops after a patient has had a heart attack. The merger will provide resources necessary to continue our Phase 3 development of CardiAMP.”



EDITAS & ADVERUM BIOTECH COLLABORATE ON DELIVERING GENE THERAPY FOR RETINAL DISEASES

The collaboration brings together Adverum’s expertise in ophthalmology and adeno-associated viral (AAV) vector development with the CRISPR gene editing capabilities of Editas Medicine to create therapies for debilitating eye diseases that have poor existing treatments.

Adverum Biotechnologies, a California-based gene therapy company focused on the discovery and development of therapeutics for retinal and rare diseases, has initiated a collaboration with Editas Medicine, for the delivery of genome editing medicines to treat up to five inherited retinal diseases.

Paul Cleveland, CEO of Adverum Biotechnologies, commented: “We are pleased to bring together our gene therapy capabilities with Editas’ CRISPR-based approach to genome editing. Our innovative vectors have the potential to deliver Editas’ genome editing components efficiently to the retina. This collaboration expands our opportunities to capitalize on our science, ophthalmology expertise and vector development know-how.”

Under the terms of the agreement, Editas will pay Adverum an upfront fee of \$1 million to evaluate Adverum’s next-generation AAV vectors for

use in clinical development. It will also pay for all preclinical activities related to this collaboration, partially via the upfront payment. Editas will also pay another \$1 million option exercise fee for each indication it chooses to pursue under this partnership. Adverum is eligible to receive development and commercial milestone payments and royalties.

Katrine Bosley, CEO of Editas Medicine, commented: “As we continue to invest in our genome editing platform, we’re delighted to collaborate with Adverum Biotechnologies on next-generation AAV vectors. Adverum brings a distinctive technology and experience base, and this collaboration aligns highly with our broader, multi-faceted delivery strategy.”



JUNO COLLABORATES WITH MSKCC & EUREKA FOR ADVANCING CAR T-CELL IMMUNOTHERAPY

Juno Therapeutics, a Seattle-based biopharmaceutical company specialized in the development of cell-based cancer immunotherapies, has entered into an exclusive license agreement with Memorial Sloan Kettering Cancer Center (MSKCC) and Eureka Therapeutics for the development of chimeric antigen receptor (CAR) cell therapies for patients with multiple myeloma. B-cell maturation antigen (BCMA), the primary target used for the development of CAR, was developed under a collaboration agreement between Eureka Therapeutics and MSKCC. The parties expect the BCMA CAR to enter clinical trials in early 2017. The financial terms

of the agreement have not been disclosed yet.

Dr Hy Levitsky, Juno’s CSO, commented: “We are optimistic that CAR T therapy can be an important component in treating patients with multiple myeloma, and we are pleased to bring additional fully-human binding domains against BCMA and other targets into our program. We believe that a multi-pronged approach may be necessary to treat multiple myeloma, and we will pursue more than one target against myeloma. The MSK and Eureka constructs are promising additions to our portfolio that will accelerate our efforts and provide additional opportunities to combat this disease.”



MULTIPLE MYELOMA SPACE GETTING HEATED

Juno therapeutics, Memorial Sloan Kettering and Eureka Therapeutics are joining forces to develop CAR therapies targeted to BCMA and other undisclosed targets for multiple myeloma. The pipeline for multiple myeloma is younger than those of the

lymphomas and leukemias, but myeloma is heating up quickly as a space within which many of the familiar names will compete. Celgene is developing a CAR therapy targeted to BCMA, which it licensed from Bluebird after it entered the clinic earlier this year, while Novartis and Cellectis have CAR-BCMA products in preclinical development. There are also some biologics of note targeted to the antigen, including an antibody-drug conjugate from GSK and bi-specific from Amgen. – *Mark Curtis*



EDITAS COLLABORATES WITH MASSACHUSETTS GENERAL HOSPITAL FOR ENGINEERED FORMS OF CAS9 NUCLEASES

Editas Medicine, a US-based genome editing company, has entered into an exclusive license agreement with Massachusetts General Hospital (MGH), for advancing CRISPR-Cas9 technology.

The license contributes to the intellectual property and technology protection related to the high-fidelity Cas9 nucleases and Cas9 PAM variants developed by MGH, which will enable Editas to expand its portfolio in using CRISPR technology with enhanced specificity for treating genetic diseases.

The improved, high-fidelity Cas9 variant *Streptococcus pyogenes* Cas9-HF1 (SpCas9-HF1) was developed by Professor Keith Joung, Editas' scientific cofounder at MGH. The study published in *Nature* (2016) demonstrated the potential of SpCas9-HF1 in significantly reducing off-target effects and proposed it as a better alternative to wild-type SpCas9 for research and therapeutic applications. The research group had also identified and

characterized several novel *S. pyogenes* and *S. aureus* Cas9 PAM variants that substantially increase the range of sites in the genome that can be targeted for genome editing. Protospacer adjacent motif (PAM) is the section of Cas9 protein that dictates where the protein can bind to DNA.

These newly identified tools will potentially enable Editas to broaden the number of target sites it could use for gene editing and could enable the company to pursue diseases that were beyond the reach of its first-generation capabilities.

Katrine Bosley, CEO of Editas, commented: "This agreement with MGH marks additional progress on our strategy of building a company committed to advancing the science behind CRISPR to benefit patients facing genetically defined diseases. These advancements align fully with our highly differentiated genome editing platform. We are eager to deploy them and unlock their therapeutic potential."



CRYOPORT & STEMEDICA EXPAND COLLABORATION FOR A STEM CELL-BASED AD TRIAL

Cryoport, a California-based cryogenic logistics company, has expanded its partnership deal with Stemedica Cell Technologies to provide cold chain logistics support for a Phase 2 clinical trial designed to assess the safety, tolerability and efficacy of allogeneic stem cell-based

therapies in the treatment of Alzheimer's disease (AD).

San Diego-based Stemedica Cell Technologies is a biopharmaceutical company specializing in the manufacturing of clinical-grade stem cells and stem cell factors for clinical trials. Currently, Stemedica's products

are used worldwide for various pre-clinical and clinical trials for acute myocardial infarction, chronic heart failure, traumatic brain injury and AD.

Under the terms of the agreement, Stemedica will have access to Cryoport's end-to-end logistics solutions including logistics management platform, shipping and condition monitoring systems to ship human stem cells from collection sites in the USA to various research centers across the country. Cryoport currently supports more than 78 clinical trials worldwide and its clients include ImmunoCellular Therapeutics, Kite Pharma, Gradalis and Perseus PCI.

Jerrell Shelton, Cryoport's CEO, commented: "Fostering strong relationships with innovative life sciences companies, such as Stemedica, is important to Cryoport and serves as an example of ongoing opportunities as new trials and product launches take place in the industry. We are proud to have worked with Stemedica since 2015 as a trusted partner distributing its ischemic-tolerant stem cell products to its wide client base within the research community. Stemedica has now evolved to the point where it is conducting a Phase 2 clinical trial and we are very pleased to scale our agreement with them to support their work fighting AD."



AVROBIO RAISES \$25 MILLION IN SERIES A FINANCING

AVROBIO, a Cambridge, MA-based clinical-stage biotechnology company specialized in the development of lentiviral-based gene therapies for rare diseases and cancer, has announced that it raised \$25 million in Series A financing. The round was co-led by Atlas Venture, Clarus and SV Life Sciences.

AVROBIO will use the funds to advance development of its clinical programs in Fabry disease and acute myeloid leukemia (AML), and to expand its portfolio in rare diseases and cancers.

The company also announced new additions to its board of directors – Bruce Booth (Partner at Atlas Venture) as chairman of the board, Scott Requadt (Managing Director at Clarus) and Joshua Resnick (MD and Partner at SV Life Sciences).

AVROBIO's initial two clinical programs are aimed to establishing

the safety and efficacy of *ex vivo* gene therapy to treat Fabry disease and AML patients, and thus improve their quality of life and life expectancy.

In AML, patients receive autologous AML cells transduced to express IL-12, whereas in Fabry disease patients receive an autologous stem cell transplantation with mobilized CD34+ cells transduced to express the enzyme alpha galactosidase A (alpha-gal A). Avrobio's technology includes a so-called 'safety system', which allows transduced cells to be eliminated by administering the anti-viral medication azidothymidine (AZT).

Geoff MacKay, AVROBIO's President and CEO, commented: "AVROBIO's highly innovative therapies offer potentially life-altering impact for patients following a single infusion of genetically



modified cells. We are grateful for the funding and support we have received from our investors, as we continue to focus on displacing the standard of care for patients with Fabry disease or AML through the development of these disruptive gene therapies.”



News that AvroBio has raised \$25 million to support early phase trials in Fabry disease and AML is interesting, as it indicates that investors are willing to support gene therapy approaches, even where there are already available therapies. Developing a gene therapy treatment for Fabry disease will be challenging, given that

there are already two parenteral enzyme replacement therapies available (albeit with a history of manufacturing and supply issues) and that Amicus Therapeutics has recently gained approval for its oral chaperone therapy in Europe. It will be interesting to see whether patients with Fabry disease will be willing to undergo the bone marrow transplant that AvroBio’s treatment requires. The early development program in Fabry disease will definitely be one to watch! – *Richard Philipson*



PLURISTEM WINS \$8 MILLION GRANT FROM EUROPE'S HORIZON 2020 PROGRAM

Pluristem Therapeutics, an Israel-based developer of placenta-based cell therapy products, has received an \$8 million grant from the EU’s Horizon 2020 program for its Phase 3 clinical trial for the treatment of critical limb ischemia (CLI). This pivotal study using Pluristem’s PLacental eXpanded (PLX)-PAD cells for the treatment of CLI is a double blind, randomized, placebo-controlled trial in which patients will be injected intramuscularly with 300 million cells. A second dose will be administered 2 months after the first. The study will be conducted in an estimated 250 patients with Rutherford Category 5 CLI who are unsuitable candidates for revascularization and the primary endpoint of the trial will be time to amputation and death.

This collaborative project will be carried out by Pluristem and

an international consortium led by the Berlin-Brandenburg Center for Regenerative Therapies under the leadership of Professors Hans-Dieter Volk and Petra Reinke. The consortium also includes leading research institutes and clinical sites in Europe.

Pluristem’s PLX-PAD program has been previously selected for the EU’s Adaptive Pathways project, the goal of which is to accelerate the development of innovative medicines for serious conditions that lack adequate treatment options.

Zami Aberman, Chairman and CEO of Pluristem, commented: “We are honored to have been awarded this Horizon 2020 grant designed to support the manufacturing and development of our cell products for potential commercialization. This grant is a vote of confidence and an expression of hope

by the EU that we may be able to provide a regenerative therapy for millions of CLI patients around the world. Pluristem is committed to developing PLX-PAD for patients

with peripheral artery disease, and this grant will help us move towards our goal of rapid entry into the European and US markets, given positive results.”



TxCell, a clinical-stage biotechnology company focused in the development of personalized T-cell immunotherapies for the treatment of severe chronic inflammatory and autoimmune diseases, has appointed Dr Olivier Danos to its scientific advisory board (SAB).

TXCELL APPOINTS BIOGEN'S DR OLIVIER DANOS TO ITS SCIENTIFIC ADVISORY BOARD

Dr Danos is the senior vice president of the cell and gene therapy program at Biogen and a renowned expert in the field of gene therapy for hematological and neurological diseases. Prior to Biogen, Dr Danos served as senior vice president at Kadmon Pharmaceuticals, director of the gene therapy consortium at UCL and led a gene therapy research team

at the Necker Hospital – Enfants Malades in Paris.

TxCell's SAB was created in March 2016 with the appointment of the first three members: Professor Zelig Eshhar (Weizmann Institute of Science, Israel), Professor Chiara Bonini (San Raffaele Hospital, Italy) and Dr Bernard Malissen (Center of Marseille-Luminy, France).

EDITAS MEDICINE APPOINTS CHARLES ALBRIGHT AS CSO

The genome editing company Editas Medicine has announced the appointment of Dr Charles Albright as its CSO. Dr Albright has over 25 years of experience in

the life sciences industry and joins Editas from Bristol-Myers Squibb, where he was the vice president of the Genetically Defined Diseases and Genomics department. Prior

to that, he held multiple scientific positions at Incyte Corporation and DuPont Pharmaceuticals and was an Assistant Professor at Vanderbilt University.

