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.

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CELL THERAPY: Kite Pharma launched its flagship manufacturing facility in El Segundo, California, in June, which will serve to manufacture autologous T cell therapies for clinical studies and for the manufacture of commercial product. The 43,500 sq ft facility is anticipated to have capacity of up to 5,000 doses per year and is strategically located next to Los Angeles International airport to expedite shipping and receiving of product. So far the two largest T cell players, Juno and Kite, have both made moves to bring manufacturing in-house. It will be interesting to see whether other key players choose to do the same. Cellectis, which is leading the race in allogeneic T cell products, chose a contract manufacturer, CELLforCURE, to carry out cGMP manufacture of UCART123 for hematological malignancies in Europe. Kite and Juno are cash rich, much more so than other competitors. So, bringing capabilities in-house was likely an easy decision. Kite will retain its contract manufacturing partners for the time being.

GENE THERAPY: Bluebird bio are in the news again this month and this time they have announced that they have agreed a long-term Commercial Manufacturing Agreement with Lonza for their Lenti-D™ and Lentiglobin™ products. It would appear that Lonza will acquire the necessary regulatory approval to manufacture and supply the gene therapy part of these two

Bluebird products when they are commercialized. This is an interesting approach to use by Bluebird as commercial manufacturing organizations (CMOs), like Lonza, have always shied away from committing to the manufacture of commercial gene therapy products when asked. Clearly now that three gene therapy-based products have been approved in Europe, with more to follow, it looks like CMOs now feel that the risk of doing this for clients has sufficiently reduced. Perhaps other CMOs will now follow and Lonza should now be congratulated at taking this bold step of being one of the first. To me this is yet another sign that gene therapy is here to stay!

saRNA FOR LIVER CANCER: MiNA THERAPEUTICS DOSES FIRST PATIENT IN PHASE 1 TRIAL

MiNA Therapeutics, a biotechnology company specializing in the development of small activating RNA (saRNA)-based therapeutics, have announced the initiation of its OUTREACH Phase 1 clinical trial to evaluate the safety and tolerability of MTL-CEBPA in treating severe liver cancer.

This first-in-human saRNA trial uses double-stranded RNA formulated into a SMARTICLES® liposomal nanoparticle and is designed to activate the *CEBPA* gene. *CEBPA* encodes for C/EBP-α, a transcription factor that plays an important role in normal liver function and its increased expression has been linked to positive outcomes in multiple pre-clinical models of liver disease.

The OUTREACH study consists of a dose escalation phase followed by a dose expansion. Dr. Debashis Sarker, Principal Investigator of the NIHR Biomedical Research Centre at Guy's and St. Thomas' and King's College London, and chief investigator of the study, commented: "MTL-CEBPA has shown great promise in pre-clinical studies in liver disease models. We are looking forward to evaluating this highly innovative therapy in the upcoming Phase I trial. We hope MTL-CEBPA could represent an important new treatment option for patients with advanced liver cancer." In the future, MiNA expects to initiate clinical trials of MTL-CEBPA in a number of diseases beyond liver cancer.

KITE PHARMA'S KTE-C19 FOR B-CELL LYMPHOMA GAINS ACCESS TO EMA'S PRIME SUPPORT

Kite Pharma has announced that KTE-C19, its CAR-T therapy has gained access to the European Medicines Agency (EMA) Committee for Medicinal Products for Human Use (CHMP) and Committee for Advanced Therapies (CAT)'s Priority Medicines (PRIME) support, for the treatment of refractory diffuse large B-cell lymphoma (DLBCL). PRIME is a new EMA initiative to provide enhanced

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scientific guidance and support accelerated review of novel investigational therapies.

Kite's KTE-C19 is an investigational therapy in which a patient's T-cells are genetically modified to express a chimeric antigen receptor (CAR) designed to target the antigen CD19, a protein expressed on the cell surface of B-cell lymphomas and leukemias. KTE-C19 was granted Breakthrough Therapy Designation by the US Food and Drug Administration (FDA) in 2015 for the treatment of DLBCL, primary mediastinal B-cell lymphoma (PMBCL) and transformed follicular lymphoma (TFL). Kite is currently enrolling patients with various B cell malignancies for four pivotal studies (also known as ZUMA studies) using KTE-C19.

Kite Pharma has also announced results of its study evaluating the effect of low-dose chemotherapy conditioning followed by anti-CD19 CAR-T therapy in the treatment of advanced non-Hodgkin lymphoma (NHL). The data presented at the *2016 American Society of Clinical Oncology (ASCO) Annual Meeting* by Dr. James Kochenderfer, an investigator in the Experimental Transplantation and Immunology Branch of the National Cancer Institute (NCI) Center for Cancer Research, showed that CAR T-cell therapy was effective in inducing a high response rate in patients with advanced NHL.

In this study of 22 NHL patients (19 diffuse large B-cell lymphoma, 2 follicular lymphoma, and 1 mantle cell lymphoma), 55% of the patients achieved complete responses and 73% gained objective responses following low-dose chemotherapy conditioning regimen. Additionally, 47% with diffuse large B-cell lymphoma and all the three patients with mantle cell lymphoma and follicular lymphoma achieved complete responses. Reversible grade 3 or 4 neurotoxicity including confusion, dysphasia, encephalopathy, and gait disturbances were observed in 55% of treated patients.

This study was performed pursuant to a Cooperative Research and Development Agreement between the NCI and Kite.

GENE THERAPY TRIAL FOR LEBER'S HEREDITARY OPTIC NEUROPATHY SHOW PROMISE

GenSight Biologics, a clinical-stage biotechnology company specialized in developing gene therapies for retinal diseases and diseases of the central nervous system (CNS), has announced promising results of its Phase I/II study, designed to evaluate the safety and tolerability of GS010 in 15 patients with Leber's Hereditary Optic Neuropathy (LHON).

LHON is a rare genetic disorder affecting the retinal ganglion cells leading to a persistent and severe bilateral loss of visual acuity within weeks or months. The disease is caused by point mutations in the mitochondrial DNA. GenSight's GS010 uses a mitochondrial targeting sequence (MTS) proprietary technology platform which, when associated with the

gene of interest, allows the platform to specifically address defects inside the mitochondria using an adeno-associated vector (AAV).

An escalating dose of GS010 was administered to each cohort of patients through a single intravitreal injection. The average onset of disease for these patients was 6 years. At 48 weeks post injection patients with a disease onset of less than 2 years showed a gain of +30 letters in the treated eye and +13 letters in the untreated eye, a difference of 17 letters in favor of the treated eye. No significant difference was observed in patients with disease onset of more than 2 years.

Bernard Gilly, CEO and co-founder of GenSight commented: "This preliminary data is very encouraging and validates the design of the two Phase III studies currently ongoing in the US and Europe on GS010 for the treatment of Leber's Hereditary Optic Neuropathy. Moreover, these results support the potential of our mitochondrial targeting sequence technology platform,or MTS, and allows us to envision other applications in diseases involving defects of the mitochondrion, in ophthalmology as well as in other therapeutic areas."

ADAPTIMMUNE THERAPEUTICS PRESENT DATA ON SPEAR™ IMMUNOTHERAPY TRIALS

Adaptimmune Therapeutics, a clinical-stage pharmaceutical company specialized in developing cancer immunotherapy products based on its Specific Peptide Enhanced Affinity Receptor (SPEAR™) T-cell platform, presented preliminary results from its immunotherapy trials at ASCO. Adaptimmune's lead candidate is a SPEAR T-cell therapy targeting the NY-ESO cancer antigen present in solid tumors and in hematologic cancer types, including synovial sarcoma and multiple myeloma. Main highlights from its three posters are summarized below:

Genetically engineered NY-ESO-1 Specific T-Cells in HLA-A:0201 positive Patients with Advanced Tumors: NY-ESO SPEAR T-cells exhibited durable persistence without the requirement for IL-2 support *in vivo*, with cells detectable for up to 3 years; the cells were well tolerated by the patients with an acceptable benefit:risk profile.

Cytokine Release Syndrome (CRS) in patients treated with NY-ESO-1c259SPEAR T cells: 15% of patients treated with NY-ESO SPEAR T-cells as of January 2016 were diagnosed with CRS. The authors concluded that the incidence of CRS with NY-ESO SPEAR T-cell therapy is of lower frequency and severity than reported with CD19 CAR-T therapy.

Targeting alpha fetoprotein (AFP) with SPEAR T-cells in hepatocellular carcinoma (HCC): AFP SPEAR T-cells recognize highly positive HCC tissue without marked recognition of non-cancerous tissue; no off-target AFP T-cell responses of concern were observed against a variety of cell types from a variety of organ systems.

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SANGAMO RECEIVES FDA CLEARANCE TO START CLINICAL TRIALS IN MPS II

Sangamo BioSciences, Inc., a US-based clinical stage biopharmaceutical company specialized in the development of therapeutic genome editing technologies, have announced the clearance of their Investigational New Drug application (IND) by the FDA for the treatment of Mucopolysaccharidosis Type II (MPSII). The IND is now active and enables Sangamo to initiate a Phase 1/2 clinical trial (SB-913-1602) to assess the safety and efficacy of SB-913, a zinc finger nuclease (ZFN)-mediated approach designed to provide a long-lasting therapy for MPS II.

Sangamo's SB-913-1602 is designed as a Phase 1/2 open-label, dose-escalation study in male subjects with MPS II. The study will evaluate the safety, tolerability and potential efficacy of a single administration of SB-913. SB-913 is formulated as AAV vector preparations encoding the therapeutic human IDS enzyme and ZFNs specific for the albumin locus, and will be administered as a single intravenous infusion.

Sandy Macrae, Sangamo's President and CEO commented: "Our gene-based approach is designed to give the patient the ability to make their own replacement enzyme and has the potential to provide significant clinical and quality of life advantages over repeatedly administered enzyme replacement therapy, which is the current standard of care for MPS II and a number of other genetic diseases. Ultimately, our target population will include pediatric patients who can benefit from a more durable solution. We believe that a ZFN-mediated genome editing approach can best serve the broadest group of MPS II patients and their families."

FDA GRANTS FAST TRACK DESIGNATION FOR FATE THERAPEUTICS' PROTMUNE™

Fate Therapeutics, a biopharmaceutical company specialized in the development of cellular immunotherapies for cancer and immune disorders, has announced that the FDA has granted Fast Track designation for ProTmune™ for the reduction of incidence and severity of acute graft-versus-host disease (GvHD) in patients undergoing allogeneic hematopoietic cell transplantation (HCT).

Fast track is a process designed to facilitate the development and expedite the review of drugs to treat serious conditions and fill an unmet medical need. The purpose is to get important new drugs into the clinic earlier. Acute GvHD occurs within a few months following HCT when the newly-transplanted donor immune cells attack the patient's tissue. Although there are several protocols to reduce the incidence

of acute GvHD, up to 50% of HCT recipients still experience the debilitating disease. Additionally, only about half of patients with acute GvHD durably respond to its treatment. There are approximately 30,000 allogeneic HCT procedures performed globally each year.

The trial is designed as an open-label, Phase 1/2 multi-center clinical study for the prevention of acute GvHD and cytomegalovirus (CMV) infection, both of which are leading causes of morbidity and mortality in patients undergoing HCT. ProTmune™'s cell therapy is produced by modulating a donor-sourced, mobilized peripheral blood graft *ex vivo* with two small molecules (FT1050 and FT4145) to enhance the biological properties and therapeutic function of the graft's immune cells. The programmed mobilized peripheral blood graft is adoptively transferred and administered to a patient as a one-time intravenous infusion.

Dr. Chris Storgard, Chief Medical Officer of Fate Therapeutics commented: "Acute graft-versus-host disease is a leading cause of morbidity and mortality in allogeneic HCT recipients. There is no approved preventive therapy, and current treatments suppress immune function and place high-risk immunocompromised patients at even greater risk for severe infections. We look forward to continuing to work with the FDA to rapidly advance our novel immunotherapy through the clinical development and regulatory processes, with the aim of bringing a transformative therapy to patients in an expedited time frame."

FIRST CRISPR CLINICAL TRIAL GETS APPROVAL FROM US PANEL

An advisory committee at the US National Institute of Health (NIH) has approved a proposal to use clustered regularly interspaced palindromic repeat (CRISPR) technology for the first time in humans to help augment cancer therapies. CRISPR technology 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 (CRISPR-associated nuclease 9) 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.

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 be funded by the Parker Institute for Cancer Immunotherapy, a $250-million foundation formed by former Facebook president Sean Parker. The University of Pennsylvania will manufacture the edited cells and will recruit and treat patients at the MD Anderson Cancer Center in Texas, and the University of California in San Francisco.

In the CRISPR procedure, researchers will remove T cells from 18 patients with several types of cancers and perform three CRISPR edits on them. The first edit

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will insert a gene for a protein engineered to detect cancer cells and instruct the T cells to target them, the second edit will remove a natural T-cell protein that could interfere with this process. The final edit is defensive and will remove the gene for a protein that identifies the T cells as immune cells and prevent the cancer cells from disabling them. The researchers will then infuse the edited cells back into the patient.

The trial proposed by scientists at the University of Pennsylvania, still needs the approval from the individual medical centers where it would be conducted as well as from the FDA. If the study gets approval from these organizations, it will enroll patients with multiple myeloma, melanoma and sarcoma.

CRISPR-Cas9-based technologies continue to make news with announcements relating to licencing collaborations, funding success and approval for use in human clinical trials. CRISPR Therapeutics and Anagenesis Biotechnologies have announced a collaboration to co-develop treatments for muscle diseases, whilst B-MoGen Biotechnologies have successfully completed Series A financing for its gene editing and gene delivery technologies. In addition, the RAC at the NIH in the USA have approved the first clinical study in patients that will use CRISPR-Cas9 technology. The study will be run at UPenn but it still awaits approval from university medical centers and the FDA before it can start. It had been rumored that Editas Medical would be the first group to get clinical study approval and that was expected next year, but it now looks like they have been beaten to the finish line. However, the views of the FDA are now needed and this will then set the mark for others to follow. It is interesting how fast this technology seems to be progressing on many fronts and all we need now is proof that it will work in humans and be safe. - *Alan Boyd*

FDA GRANTS ORPHAN DRUG DESIGNATION TO WAVE'S HUNTINGTON'S DISEASE PRODUCT

WAVE Life Sciences Ltd., a US-based pharmaceutical company specialized in developing nucleic acid-based therapeutics for rare diseases, has received orphan drug designation from the FDA for their product WVE-120101, developed for the treatment of Huntington's disease (HD). Orphan drug designation is granted by the FDA Office of Orphan Products Development to novel drugs or biologics that treat a rare disease or condition affecting fewer than 200,000 patients in the USA and will entitle 7 years of market exclusivity.

HD is an autosomal dominant, progressive neurodegenerative disease that causes the progressive breakdown of nerve cells in the

brain. WVE-120101 targets a single nucleotide polymorphism that is associated with the disease-causing mutation in the *huntingtin* (*HTT*) gene. WAVE's approach enables selective silencing of the disease-causing HTT allele, while leaving the healthy HTT allele to produce normally functioning protein.

Dr. Paul Bolno, President and CEO of WAVE commented: "We are pleased to receive Orphan Drug Designation for our first Huntington's disease therapy and to advance what may be the first allele-targeted therapy into clinical trials, particularly as there are no approved disease-modifying treatments for HD. WVE-120101 is the first of our two lead allele-specific antisense programs for HD, and we are on track to file investigational new drug (IND) applications for both in late 2016."

AGILIS BIOTHERAPEUTICS WINS NCATS'S CRADA FOR RESEARCH ON RARE DISEASES

Agilis Biotherapeutics, a biotechnology company focused on developing gene therapies for rare diseases of the CNS, has been selected by the National Center for Accelerating Translational Sciences (NCATS) as an awardee of a Cooperative Research and Development Agreement (CRADA) under the NIH's Therapeutics for Rare and Neglected Diseases (TRND) program.

Aromatic L-Amino Acid Decarboxylase (AADC) deficiency is a rare-genetic disease affecting the biosynthesis of serotonin, dopamine and catecholamines. It can result in profound developmental failure, frequent hospitalizations, life-long care and premature death. Agilis' AADC gene therapy was developed by Dr. Paul Hwu and team at the National Taiwan University. Results obtained from 18 treated patients showed significant improvement in their motor and cognitive function over multiple years. The Agilis-TRND partnership will conduct toxicology, process development and manufacturing work necessary for the development of this therapeutic, and conduct registration in the USA and abroad.

Applicants to the TRND program go through a competitive process of selection whereby the TRND scientists select the most promising proposals for the prestigious public–private partnership. The mission of the TRND program is to use NIH resources to encourage and accelerate the development of new treatments for rare diseases. As the first gene therapy company selected for this collaborative program, the partnership merges Agilis' expertise with the NIH's scientific team, development experience, and overall intramural resources to expedite this much needed treatment for patients with AADC deficiency. The partnership could potentially be worth up to several million dollars to Agilis in in-kind services and activities from NIH.

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VM BIOPHARMA INITIATES A PHASE 3 GENE THERAPY TRIAL FOR DIABETIC PERIPHERAL NEUROPATHY

VM Biopharma, a US-based biopharmaceutical company has dosed the first patient in a recently initiated Phase 3 gene therapy clinical trial to evaluate the efficacy of VM202 in patients with painful diabetic peripheral neuropathy (DPN). DPN, a neuronal disorder, is a common complication of diabetes in which nerve damage results in sudden and severe pain. It affects 5–20% of diabetes patients and currently there are no treatments for the disease. The VM202 trial is the first pivotal gene therapy study specifically targeting the most common cause of severe neuropathy, and follows the successful completion of a Phase 2 trial conducted at Northwestern University and multinational sites in the US and Korea.

The VM202 Phase 3 trial is designed as a double-blind, randomized, placebo-controlled, multi-center study to determine the safety and efficacy of bilateral intramuscular injections of VM202 versus placebo in the treatment of painful diabetic neuropathy. A total of 477 subjects will be randomized in a 2:1 ratio to either VM202 (n = 318) or placebo (n = 159). The primary clinical efficacy outcome will be the change in average pain score from baseline to the 3-month follow-up visit, as well as a 50% responder rate. The study is expected to complete in October 2018.

VM202 is a plasmid DNA that contains a genomic cDNA hybrid human hepatocyte growth factor (HGF) coding sequence, expressing both isoforms of HGF simultaneously. HGF is a growth factor that induces angiogenesis and acts as a neurotrophic factor to peripheral nervous system. Intramuscular administration of VM202 was shown to provide significant symptomatic relief to patients with DPN. VM202 is believed to promote microvasculature and regenerate nerve cells, providing clinical benefit to patients with DPN.

EXPERT PICK

VM Pharma have announced the initiation of a Phase 3 study evaluating their gene therapy product, VM202, for the treatment diabetic peripheral neuropathy. This follows on from the reporting of their successful results from a Phase 2 study which demonstrated a significant reduction in pain in patients suffering from this disease. The transgene in the product is the human growth factor (HGF) gene that is known to induce angiogenesis and also act as a neurotrophic factor to the peripheral nervous system. The current treatment approaches for this condition are mainly for symptomatic relief only and do not affect the underlying pathology. The company have claimed that VM202 has shown signs that it may elicit a disease-modifying effect so the results of this Phase 3 study will be awaited with interest. - ***Alan Boyd***

OXFORD BIOMEDICA & GREEN CROSS LABCELL COLLABORATE TO DEVELOP CELL-BASED THERAPEUTICS

Oxford BioMedica plc, a UK-based cell and gene therapy company, has entered into a research & development collaboration with Green Cross LabCell (GCLC) for the identification and development of genetically engineered natural killer (NK) cell-based therapeutics for treatment of life-threatening diseases such as cancer.

Green Cross LabCell, a subsidiary of Korea-based pharmaceutical company Green Cross Corp, is specialized in developing next generation gene-modified NK cell therapeutics. Oxford BioMedica is contributing its clinically tested LentiVector® gene delivery platform for the efficient modification of immune cells, expertise in GMP bioprocessing, clinical development and regulatory affairs in *ex vivo* cell & gene therapy. GCLC is contributing its clinically tested platform for production of highly potent and activated NK cells.

Under the terms of the agreement, Oxford BioMedica & GCLC will equally share the costs associated with the research collaboration. Oxford BioMedica's contribution to the research collaboration will be funded from its existing discovery resources and budget.

John Dawson, CEO of Oxford BioMedica commented: "We are very excited to form a key partnership with Green Cross LabCell, who have the industry-leading production platform for NK cell therapeutics for cancer. Over the years Green Cross LabCell has built a significant depth of scientific, technical and industrial expertise in NK cells that is difficult to find elsewhere. We are therefore delighted to be collaborating with Green Cross LabCell in a new partnership which brings our LentiVector® delivery platform and expertise to the relationship and which builds on our existing partnerships with other companies including Novartis, Sanofi, GSK and Immune Design. We believe that our collaboration will lead to the generation of a rich pipeline of novel gene-modified NK cell therapeutics for both companies."

In a second announcement this this month, Oxford BioMedica has entered into a non-exclusive licence agreement with MolMed. Under the terms of the agreement, Oxford BioMedica will give MolMed the right to use its LentiVector® platform technology patents for manufacturing and development services. A previous retroviral patent agreement between Oxford BioMedica and MolMed has now expired.

ADAPTIMMUNE ENTERS 10-YEAR AGREEMENT WITH THERMO FISHER

Adaptimmune Therapeutics has entered into a 10-year commercial development and supply agreement with Thermo Fisher Scientific for the latter's Dynabeads CD3/CD28 Cell Therapy System (CTS™) for use in the manufacture of Adaptimmune's SPEAR™ T-cell therapies.

Dynabeads™ CD3/CD28 CTS provides coordinated and

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simultaneous activation and co-stimulation signals to T-cells, a process that is reported to produce T-cells with enhanced proliferation capability. Adaptimmune has an exclusive license for the intellectual property associated with the use of Dynabeads CD3/CD28 to expand and activate all TCR-transduced T-cells in cancer, infectious and autoimmune diseases.

The manufacturing process consists of isolating T-cells from the blood of cancer patients; transferring affinity enhanced TCRs into the cells; activating and expanding the T-cells using Dynabeads CD3/CD28; and finally, introducing the affinity enhanced cells back into the patient to enable the patient's immune system to respond and attack cancer.

KITE ENTER RESEARCH AGREEMENT WITH CELL DESIGN LABS

Kite Pharma have entered into a research collaboration and license agreement with Cell Design Labs, to develop next generation, precision-controlled CAR product candidates that incorporate Cell Design Labs' molecular "on/off switch" technology. The technology employs small molecule-mediated protein dimerization domains to switch CAR products on/off. Through this technology, physicians will have the potential to rapidly control and reversibly titrate the activity of CAR T-cells. Under the terms of the agreement, Kite will pay Cell Design Labs an upfront payment and additional payments to support Cell Design Labs' research.

Kite Pharma has also officially opened a new commercial manufacturing facility in El Segundo, California. This 43,500-square-foot plant is designed to produce CAR and T-cell receptor product candidates for clinical trials and for the potential launch and commercialization of KTE-C19. The facility is estimated to have the capacity to produce up to 5,000 patient therapies a year. The plant is located near to Los Angeles International Airport and is intended to accelerate the receipt and shipment of engineered T-cells from and to patients across the US and Europe.

MOLECULAR "ON/OFF" SWITCHES MOVING TOWARDS CLINIC

Kite Pharma and Cell Design Labs announced a deal to bring molecular "on/off" switches into Kite's product pipeline. Cell Design Labs' platform focuses on protein dimerization using available small molecule compounds, which functionally activates CARs in vivo. This technology is an alternative to suicide genes, which allow for destruction of a dose of cells following administration of a small molecule. However, the switch approach comes with the added benefit of being able to titrate down the concentration of CAR; advantageous if you want to ratchet back unwanted effects without eliminating therapeutic cells entirely. Kite will have exclusive, worldwide rights to Cell Design's technology for use in AML, and rights to the technology for certain targets in B cell malignancies. Kite will make a further investment in the company of $6 million. Cell Design Labs could earn as much as $67.5 million from the deal. -***Mark Curtis.***

CRISPR THERAPEUTICS & ANAGENESIS COLLABORATE ON CRISPR/CAS9-BASED CELL THERAPIES FOR MUSCLE DISEASES

In a move towards advancing CRISPR/Cas9-based cell therapies, CRISPR Therapeutics and Anagenesis Biotechnologies have entered into a strategic in-licensing and collaboration agreement, which grants CRISPR Therapeutics exclusive worldwide license to Anagenesis' Paraxial Mesoderm Multipotent Cells (P2MC) technology for the treatment of musculoskeletal diseases. The initial research will focus on Duchenne Muscular Dystrophy (DMD).

The P2MC technology which was developed with the support of AFM-telethon, INSERM-Transfert, CNRS and Université de Strasbourg, enables the differentiation of pluripotent cells into skeletal muscle stem cells, also known as satellite cells. Combining P2MC with CRISPR/Cas9 gene editing has the potential to yield important new treatments for patients with muscle disorders.

Dr. Bill Lundberg, Chief Scientific Officer of CRISPR Therapeutics commented: "Bringing together the CRISPR gene editing platform with the P2MC technology enables us to develop ex vivo therapeutic approaches for the treatment of DMD using muscle satellite stem cells".

SORRENTO SUBSIDIARY - TNK THERAPEUTICS - & 3SBIO CAR-T COLLABORATION

Sorrento Therapeutics, a clinical-stage biopharmaceutical company developing antibody-based treatments, has announced that its subsidiary TNK Therapeutics has entered into a joint venture agreement with Shenyang Sunshine Pharmaceutical Company (3SBio) to develop and commercialize its proprietary immunotherapies, including CAR-T technology targeting carcinoembryonic antigen (CEA) positive cancers. 3SBio is a China-based biotechnology company focused on discovering, developing, manufacturing, and commercializing biopharmaceutical products. Under the terms of the agreement, 3SBio will pay $10 million to the joint venture and TNK will grant an exclusive license to the CEA CAR-T technology and two additional CARs for cellular therapy for the Greater China market.

Dr. Henry Ji, President and CEO of Sorrento commented: "We are pleased that 3SBio, a leading biotechnology company in China, has recognized the value of our CAR-T technologies and we look forward to working with them to advance the development of our novel anti-cancer cellular therapies".

In additional news this month, Sorrento has also announced the completion of a $150 million financing round related to the private placements of common stock and warrants. All warrants issued

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have a term of three years and an exercise price of $8.50 per share. Proceeds from the financing will be majorly used to support the development of Sorrento's product pipeline and for general corporate purposes.

Ally Bridge Group, a global healthcare-focused investment group based in Hong Kong, led the financing round and together with Beijing Shijilongxin Investment and Frejoy investment management groups have collectively purchased 25,225,221 shares of common stock at $5.55 per share, and warrants to purchase 5,055,642 shares of common stock for total consideration of $140 million.

LONZA & BLUEBIRD SIGN COMMERCIAL MANUFACTURING AGREEMENT FOR LENTI-D™ & LENTIGLOBIN™ PRODUCTS

Lonza has entered into a strategic manufacturing agreement with Bluebird bio to provide future commercial production of bluebird bio's Lenti-D™ and LentiGlobin™ drug products. Bluebird bio is a clinical-stage company specialized in developing T-cell based immunotherapies.

This agreement follows a successful multi-year clinical manufacturing relationship and provides bluebird bio with a path to commercial supply including dedicated production suites within Lonza's state-of-the-art facility. This facility is currently under construction, for the clinical and commercial supply of viral vectors and virally-modified cell therapy products. Lonza will complete the suite design, construction and validation along with process validation prior to anticipated commercial launch.

SORRENTO RECEIVES NEW INVESTMENT & TARGETS CHINA

Sorrento Therapeutics, a company that was once solely antibody-centric, has leveraged its expertise to tap into the CAR market. It made a strategic investment into Conkwest (now NantKwest) in December of 2014 giving it exposure to CAR-NK technology, and then went on to form a subsidiary, TNK Therapeutics, which recently acquired the rights to CAR-T technologies for use in solid tumors. The company continued its foray into adoptive cellular therapy with a joint venture announced this past month with China-based Shenyang Sunshine Pharmaceutical Company (3SBio). Under the terms of the deal 3SBio will put forth $10 million in investment and TNK Therapeutics will provide exclusive access to its CAR-T technology targeting carcinoembryonic antigen (CEA) in solid tumors. The collaboration expands Sorrento's reach directly into the Chinese market. In addition, Sorrento raised $150 million in funds via private placement from financial and strategic investors in Hong Kong and elsewhere in Asia, which will further strengthen ties to the Asian market. - *Mark Curtis*

ARGOS THERAPEUTICS AND ADAPTIVE BIOTECHNOLOGIES COLLABORATE ON IMMUNOTHERAPIES

Argos Therapeutics, a US-based immuno-oncology company focused on the development and commercialization of personalized immunotherapies for the treatment of cancer based on its Arcelis® technology platform, has signed a strategic research agreement with Adaptive Biotechnologies Corporation, to study immune response patterns to Argos' investigational immunotherapies.

Under the terms of the agreement, Adaptive will use its patented immune profiling immunoSEQ® assay to perform detailed characterization of the immune responses induced by Argos's product candidates, AGS-003 and AGS-004. The immunoSEQ assays can identify millions of T- and B-cell receptors from a single sample in exquisite detail. AGS-003 is currently being evaluated in the pivotal ADAPT Phase 3 clinicaltrial for the treatment of metastatic renal cell carcinoma and AGS-004 is being studied in an investigator-initiated Phase 2 clinical trial for HIV eradication in adult patients.

Dr. Charles Nicolette, chief scientific officer of Argos commented: "We are very excited to be entering into this important research agreement with Adaptive Biotechnologies. Adaptive is our preferred partner because of their established expertise in offering high-throughput immune receptor repertoire characterization and advanced bioinformatics that are ideally suited to analyze precision of target-specific immune activation enabled by Arcelis administration with higher resolution."

B-MOGEN COMPLETES SERIES A FINANCING

B-MoGen Biotechnologies, Inc., a spin-off company founded by two faculty members at the University of Minnesota, have announced that it has successfully completed its Series A financing with Bio-Techne and University of Minnesota's Discovery Capital Investment Program co-leading the investment round. Mayo Clinic Ventures and Lateral Capital also participated in the financing round.

US-based B-MoGen Biotechnologies, Inc. is specialized in genome editing and gene delivery in the search of non-viral techniques for the advancement of cellular therapeutics. Additionally, B-MoGen has also partnered with Mayo Clinic for mitochondrial gene editing technology.

Jeff Liter, Chief Executive Officer of B-MoGen Biotechnologies commented: "We are pleased and excited to have such a broad base of support in our Series A financing and to be working with Bio-Techne in deploying our gene editing technology in an innovative effort to improve certain Bio-Techne products. Moreover, B-MoGen technology has tremendous therapeutic potential as we optimize our methods for non-viral gene delivery into primary cells."

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BIOGEN APPOINTS PAUL MCKENZIE AS EXECUTIVE VP PHARMACEUTICAL OPERATIONS & TECHNOLOGY

Biogen has announced the appointment of Paul McKenzie as Executive Vice President of Pharmaceutical Operations & Technology. He replaces John Cox who is now chief executive officer of a new Biogen spin-off company dedicated to advancing treatments for hemophilia. Dr. McKenzie has over 30 years' experience in drug product development and joins Biogen from Johnson & Johnson (J&J), where he was vice president of R&D for J&J's Ethicon business. Prior to that, Dr. McKenzie held various R&D and manufacturing positions at Janssen, Bristol-Myers Squibb and Merck.

LION BIOTECHNOLOGIES APPOINTS NEW CEO

Lion Biotechnologies, a clinical-stage biopharmaceutical company specialized in the development of cancer immunotherapies, has announced the appointment of Dr. Maria Fardis as President and CEO. Dr. Fardis succeeds Dr. Elma Hawkins, who will continue as advisor to the board of directors.

Dr. Fardis has extensive experience in drug development and novel cancer treatments. She was formerly chief operating officer at Acerta Pharma and prior to that she held various scientific and management positions at Pharmacyclics LLC and Gilead Sciences.

SANGAMO BIOSCIENCES NAMES ALEXANDER MACRAE AS NEW PRESIDENT & CEO

Sangamo BioSciences, a clinical stage-biopharmaceutical company specialized in genome editing, has appointed Dr. Alexander Macrae as its new President and CEO following the retirement of Edward Lanphier. Edward Lanphier will continue as a member of the board.

Dr. Macrae has extensive experience in clinical research, product and business development. Most recently he served as global medical officer of Takeda Pharmaceuticals. Prior to that, he held various R&D positions at Smith Kline Beecham and GSK, where his last role was as Senior Vice President, Emerging Markets R&D.

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