Commercial insight: cell and gene therapy

DEC 2016

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
Richard Philipson
Chief Medical Officer,
Trizell Ltd, UK

CELL THERAPY
Mark Curtis
Financial Portfolio Manager,
Emerging Technologies
Lonza AG
Switzerland

GENE THERAPY: This month sees a series of encouraging news items for patients with inherited blood diseases, and gives a good indication of the high level of scientific and clinical activity in the field. Kiadis Pharma has initiated a Phase 1/2 clinical trial with its immuno-therapeutic treatment used as an adjunct to hematopoietic stem cell transplantation in beta-thalassemia major. In addition, Calimmune has announced a license agreement with Cincinnati Children's Hospital Medical Center to develop and commercialize gene therapy for sickle cell disease and beta-thalassemia. Finally, Spark Therapeutics continues its steady stream of positive pipeline news, with very encouraging preliminary data from a Phase 1/2 study indicating clinical benefit for patients with hemophilia B (factor IX deficiency) treated with its AAV vector, with a marked reduction in requirement for factor IX infusions seen in all nine patients treated.

CELL THERAPY: Kite was in the spotlight on multiple fronts at the end of 2017. The company announced rolling submission with the US Food and Drug Administration

(FDA) of its BLA for axicabtagene ciloleucel (formerly KTE-C19) in patients with relapsed or refractory B-cell non-Hodgkin lymphoma, an 82% complete remission rate in the preliminary analysis of its ZUMA-3 and ZUMA-4 studies, and a partnership with Vitruvian Networks, a move in preparation for commercial scale manufacture of autologous cell-based immunotherapy products. Vitruvian was formed by GE Ventures and the Mayo Clinic, and brings together expertise in cloud computing and data analytics to improve the ease of moving therapeutic product following FDA approval. Kite and Vitruvian will work together to create Kite Konnect, a platform to synchronize physicians, patients and treatment centers, and ensure safety and quality requirements are met. The partnership is an exciting development, not just for Kite, but for the field, as it signifies we are getting closer to the realization of implementing cell-based immunotherapy products in a commercial framework.

SPARK'S PHASE 1/2 TRIAL SHOWS POSITIVE OUTCOME IN HEMOPHILIA B PATIENTS

Spark Therapeutics and Pfizer have announced preliminary efficacy data of its Phase 1/2 trial for the treatment of hemophilia B, a rare genetic bleeding disorder. Data was presented by the lead investigator of the study, Dr Lindsey George of the Children's Hospital of Philadelphia, at the *58th American Society of Hematology (ASH) Annual Meeting*, in San Diego.

This ongoing Phase 1/2 clinical trial of SPK-FIX is designed to determine the safety and kinetics of a single intravenous infusion of SPK-9001 in hemophilia B patients. SPK-9001 is a recombinant adeno-associated virus vector carrying a high specific activity human factor IX (FIX) variant. The vector is designed to deliver *FIX* gene to the liver cells where FIX is normally made.

Preliminary data showed that all nine participants who received the treatment have reduced infusions of factor IX concentrates by 99% over cumulative 1650 days. Seven infused participants who have progressed to at least 12 weeks post-vector administration have a mean steady-state factor IX activity level greater than 28%. The first participant to reach 1 year in the study, who has been followed for 52 weeks post-infusion of *SPK-9001*, has reduced his number of intravenous factor IX infusions to zero without having any bleeds. No participants experienced thrombotic events after *SPK-9001* administration and no serious adverse events have been reported.

Spark Therapeutics and Pfizer entered a collaboration in 2014 for the SPK-FIX program, including *SPK-9001*, under which Spark Therapeutics is responsible for conducting all Phase 1/2 studies for any product candidates, while Pfizer holds responsibility for pivotal studies, any regulatory activities

DOI: 10.18609/cgti.2016.078

and global commercialization of any products that may result from the collaboration. *SPK-9001* has received breakthrough therapy and orphan product designations from FDA.

Dr Katherine A High, President and CSO of Spark, noted: "While continued observation and larger cohorts are needed, these updated preliminary data continue to be encouraging and suggest the potential of investigational *SPK-9001* to deliver a consistent, sustained and therapeutically meaningful level of factor IX activity through a one-time intravenous administration."

As the researchers continue to monitor patients in the current trial, the next steps will be to discuss with the FDA the outlines of a larger, Phase 3 clinical trial.

AGILIS' GENE THERAPY CANDIDATE RECEIVES ORPHAN DESIGNATION IN THE EU

Agilis Biotherapeutics, a US-based biotechnology company specialized in the development of gene therapies for rare genetic diseases of the CNS, has received orphan medicinal product designation from the European Commission (EC) for its gene therapy candidate AGIL-AADC, developed for the treatment of aromatic L-amino acid decarboxylase (AADC) deficiency.

AADC deficiency is a rare genetic condition arising from a deficiency in AADC, which catalyzes the final step in the synthesis of the neurotransmitters, dopamine and serotonin. AADC deficiency is caused by mutations in the dopa decarboxylase gene.

The AGIL-AADC trial is currently being performed under the direction of Dr Wuh-Liang Hwu at the National Taiwan University Hospital. AGIL-AADC is an adeno-associated virus (AAV) vector containing the human gene for the AADC enzyme. It is the first therapeutic candidate to receive orphan designation for AADC deficiency in Europe.

The EC's approval follows a positive opinion in October from the EMA's Committee for Orphan Medicinal Products (COMP). AGIL-AADC have also received Orphan Drug Designation and Rare Pediatric Disease (RPD) designation from the US FDA, giving it access to FDA's priority review pathway and the ability to qualify for a Priority Review Voucher (PRV) upon marketing approval of AGIL-AADC.

Mark Pykett, President and CEO of Agilis, commented: "Receiving orphan status from the EC, in conjunction with the previous orphan drug designation and rare pediatric disease designation from the US FDA, is another step on our path to bringing this important new medicine to patients in need of an effective, durable treatment. The orphan designation in Europe provides important benefits during development and commercialization, and represents important progress as we seek to bring this novel treatment for AADC deficiency to the market."

KITE TOGETHER WITH NCI PUBLISHES RESULT OF T CELL IMMUNOTHERAPY

Kite Pharma, a California-based biopharmaceutical company specialized in the development of cancer immunotherapy products, has published the positive result of its T cell therapy targeting mutant KRAS in a colorectal cancer patient.

KRAS is one of the most mutated genes in human cancer. *KRAS* mutations are thought to drive 95% of all pancreatic cancers and 45% of all colorectal cancers. The G12D mutation is the most common *KRAS* mutation and is estimated to occur in more than 50,000 new cases of cancer in the USA each year.

Kite entered a Co-operative Research and Development Agreement (CRADA) with the National Institutes of Health (NIH) in September 2016, to advance the development of T cell receptor (TCR)-based product candidates for the treatment of tumors expressing mutated KRAS antigens. These TCR product candidates were developed in the laboratories of Professors Steven A Rosenberg and James C Yang.

In the latest research study published in the *New England Journal of Medicine*, Professor Rosenberg and team has described a patient with KRAS mutant metastatic colorectal cancer who was successfully treated with T cells that are reactive to *KRAS* G12D mutation. The team observed objective regression of all seven lung metastases after the infusion of tumor-infiltrating lymphocytes that specifically targeted *KRAS* G12D.

Dr David Chang, Kite's CMO and Executive VP of R&D, commented: "We are very excited to see the results of this landmark study conducted by Dr Rosenberg and his team at the NCI. These findings represent proof of concept that T-cell technology directed against neoantigens can be utilized to treat solid tumors."

VOYAGER'S GENE THERAPY DATA OFFERS HOPE TO PARKINSON'S PATIENTS

Voyager Therapeutics, a Cambridge, MA-based clinical-stage company developing gene therapies for central nervous system (CNS) disorders, has announced positive interim data of its ongoing Phase 1b trial of VY-AADC01 for the treatment of Parkinson's disease.

Parkinson's disease is a neurodegenerative disorder involving loss of neurons that release dopamine in the striatum. Levodopa medication is the standard treatment prescribed to patients to compensate for the loss of dopamine. Levodopa is converted to dopamine by the enzyme AADC. As Parkinson's disease progresses, levodopa therapy becomes less effective and is associated with motor fluctuations, involuntary movements and other complications.

DOI: 10.18609/cgti.2016.078

The present VY-AADC01 trial is designed to evaluate the safety of increasing AADC levels in the striatum via *AADC* gene delivery. The human *AADC* gene is inserted into an adeno-associated viral (AAV2) vector and is injected directly into the striatum during a neurosurgical procedure that is performed with real-time MRI imaging to monitor delivery. Subjects continue to take Parkinson's disease medications, including levodopa.

The safety and potential clinical responses to VY-AADC01 was assessed by repeated clinical evaluations of Parkinson's disease, cognitive tests, laboratory blood tests and neuroimaging. The trial includes four cohorts: an initial cohort received 7.5 x 10^{11} vector genomes of VY-AADC01 and a second cohort received 1.5 x 10^{12} vector genomes. The third set of patients will receive 4.7x 10^{12} and the fourth cohort will receive the highest dose of 8.8 x 10^{12} vector genomes.

The interim data from cohorts 1 and 2 of the present gene therapy trial demonstrated that precise MRI-guided delivery of VY-AADC01 was well tolerated and resulted in increased AADC enzyme activity, enhanced response to levodopa and dose-related, clinically relevant improvements in patients' motor function. Among the five patients in cohort two, AADC activity rose by 56% and levodopa dosages fell 34% over the first 6 months of the study. These effects were maintained and in some patients improved at 12 months of follow-up.

Voyager will continue the dose escalation trial with cohort 3 enrollment expected to complete in early 2017. The company intends to update 6-month interim data from this cohort and long-term efficacy data from cohorts 1 and 2 in mid-2017. Following the news, Voyager's shares have increased 35% in after-hours trading.

ISCO RESTARTS STEM CELL THERAPY FOR PARKINSON'S DISEASE

International Stem Cell Corp. (ISCO), a California-based clinical-stage company has announced that the first two patients in its Phase 1 trial for Parkinson's disease has successfully undergone intracranial neural stem cell transplantation.

Parkinson's disease is a neurodegenerative disorder involving loss of neurons that release dopamine in the striatum. Levodopa medication is the standard treatment prescribed to patients to compensate for the loss of dopamine.

ISCO had treated the first patient in July, but additional surgical procedures were delayed by "a supply chain disruption of equipment critical to the operation," according to Russell Kern, ISCO's CSO.

The present Phase 1 study is designed as a single arm, open-label study to evaluate the safety and tolerability of ISC-human parthenogenetic neural stem cells (hpNSC) injected intracerebrally into the striatum and substantia nigra of

patients with Parkinson's disease. The study will enrol 12 patients at three dosing regimens: four patients each for the three different doses. The primary endpoint of the study is safety but will also gather preliminary efficacy data measured at six and 12 months following the treatment. The trial conducted at the Royal Melbourne Hospital in Australia is expected to complete in 2018.

Patients in the study will be treated with 30–70 million stem cells, delivered via intracranial injection. The company will use data obtained from the study to design a future Phase 2 trial, which is expected to initiate in late 2017 or 2018.

KIADIS PHARMA RECEIVES APPROVAL TO INITIATE A PHASE 1 TRIAL IN THE UK

The Medicines and Healthcare products Regulatory Agency (MHRA), UK's regulatory body, has granted approval to Amsterdam-based Kiadis Pharma, to initiate a Phase 1/2 clinical trial in the UK with its product ATIR201™ in thalassemia patients. The study has also received approval from the Ethics Committees of the Royal Manchester Children's Hospital and the Birmingham Children's Hospital, where the trial will be conducted.

Kiadis Pharma is a clinical-stage biopharmaceutical company focused in developing cell-based immunotherapy products for treating blood cancers and inherited blood disorders. ATIR201™ is developed as an adjunctive immunotherapeutic on top of allogeneic hematopoietic stem cell transplantation. This is intended to provide the patient with a functional and mature immune system that can fight infections while not eliciting severe graft-versus-host-disease (GVHD), thereby bridging the time until the immune system has fully re-grown from stem cells in the transplanted graft.

The trial will evaluate the safety and feasibility of using ATIR201™ in pediatric and adult patients suffering from beta-thalassemia. A total of up to ten patients will be enrolled and the company expects to get the initial safety and efficacy results in the second half of 2017.

The news that Kiadis Pharma has regulatory approval to start a Phase 1/2 clinical trial in beta-thalassemia major offers the prospect of a new treatment option in this serious disease. ATIR201 is used as an adjuvant to a partially T-cell depleted haploidentical hematopoietic stem cell transplant and is intended to reduce the significant risk of GVHD seen in patients who receive haploidentical transplants. If the treatment works, this opens up a wider potential pool of bone marrow donors in beta-thalassemia, since haploidentical parents can be considered if better-matched sources of bone marrow are not available. Data from the related product ATIR101 in AML and ALL already look encouraging, with lower than expected rates of GVHD in patients receiving the treatment.– *Richard Philipson*

DOI: 10.18609/cgti.2016.078

JUNO DEFEATS KITE'S CHALLENGE OVER CAR-T CELL PATENTS

Juno Therapeutics has announced that it has defeated Kite Pharma's attempt to invalidate a patent exclusively licensed by Juno, which includes a CAR-T cell therapy used for the treatment of B-cell malignancies. Juno plans to sue Kite, seeking a declaratory judgment that Kite's lead product candidate, KTE-C19, will infringe the patent when commercially produced.

Kite Pharma had filed an *inter partes* review in the US Patent and Trademark Office (USPTO) in August 2015 to invalidate Juno's CAR-T cell therapy and challenging all of its claims. Juno exclusively licenses the '190 patent, titled *Nucleic Acids Encoding Chimeric T Cell Receptors*, from Sloan Kettering Institute for Cancer Research. The patent covers, among other things, a construct for a CD-19 targeted CAR-T cell treatment that employs a CD28 costimulatory domain.

The USPTO instituted a review of the patent and issued a final written decision upholding all the claims of the patent in December 2016.

Bernard J Cassidy, General Counsel of Juno Therapeutics, commented: "We are obviously pleased by the USPTO's decision to uphold the patent. Our efforts to amicably and reasonably resolve the dispute Kite initiated have been thwarted and today we are taking the next step towards fully resolving matters. Importantly, our filing will not prevent continued patient access while the legal dispute continues."

EXPERT PICK

Juno and Kite IP Battle

In 2015, Kite filed a petition with the USPTO to challenge a narrow patent directed to CAR products containing a pre-specified CD28 co-stimulatory domain. The patent was generated by Sloan Kettering and later licensed by Juno. It was recently announced that the USPTO will uphold the patent. While Kite will appeal the USPTO decision, Juno has made a move to sue Kite seeking a judgment that axicabtagene ciloleucel (KTE-C19) will infringe its IP once it becomes marketed commercially. The proceedings will not impact patient access to the therapy. However, it could have implications for Kite's topline if Juno is successful. – Mark Curtis

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 CNS, has announced additional promising results of its Phase 1/2

study, designed to evaluate the safety and tolerability of GS010 in 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 that, 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 three patients through a single intravitreal injection in the eye most severely affected by the disease. The average onset of disease for these patients was 6 years. At 78 weeks post-injection, patients demonstrated sustainable visual acuity improvement as evidenced by a gain of +30 letters in the treated eye and +15 letters in the untreated eye, a difference of 15 letters in favor of the treated eye.

In patients with a disease onset of less than 2 years, a mean gain of +32 letters was observed in treated eyes, while a mean gain of +12 letters was observed in untreated eyes, resulting in a difference of 20 letters in favor of treated eyes. This set of patients demonstrated a positive treatment effect from week 36 onwards.

GenSight Biologics is currently conducting two Phase 3 clinical studies (RESCUE and REVERSE) in Europe and the USA to assess the efficacy of GS010 in patients affected with LHON due to the *ND4* mutation.

Bernard Gilly, CEO and co-founder of GenSight, commented: "We are very encouraged by the latest results indicating a sustainable clinical benefit for patients in this long-term follow-up. This data continues to support the design of our two Phase 3 studies with GS010 for the treatment of LHON, which are currently ongoing in the US and Europe."

KITE INITIATES BLA FILING FOR ITS CAR-T THERAPY

Kite Pharma has initiated the rolling submission of the Biologics License Application (BLA) with the FDA for KTE-C19 as a treatment for patients with relapsed/refractory aggressive B-cell non-Hodgkin lymphoma (NHL) who are ineligible for autologous stem cell transplant (ASCT). The company expects to complete its BLA submission by early 2017.

KTE-C19, Kite's lead product candidate, is an investigational therapy in which a patient's T cells are genetically modified to express a chimeric antigen receptor designed to target the antigen CD19, a protein expressed on the cell surface of B-cell lymphomas and leukemias.

The ZUMA-1 trial that supports the BLA submission enrolled patients with three subtypes of aggressive NHL: chemorefractory diffuse large B-cell lymphoma (DLBCL), transformed follicular

DOI: 10.18609/cgti.2016.078

lymphoma (TFL) and primary mediastinal B-cell lymphoma (PMBCL).

Kite also announced that the United States Adopted Name, or USAN, for KTE-C19 will be axicabtagene ciloleucel.

KTE-C19 was granted Breakthrough Therapy Designation by the FDA in 2015 for the treatment of DLBCL, PMBCL and TFL. It also gained access to the European Medicines Agency (EMA)'s Priority Medicines (PRIME) support, for the treatment of DLBCL earlier this year.

If the present application is approved, Kite plans to commercially launch KTE-C19 in 2017. The company also intends for a regulatory submission to the EMA this year.

JUNO'S AND CELGENE'S CELL THERAPY CANDIDATE RECEIVES APPROVAL FROM FDA AND EMA

Juno Therapeutics' and Celgene Corporation's investigational drug JCAR017 has been granted Breakthrough Therapy Designation from the FDA and Priority Medicines Eligibility (PRIME) from the EMA for the treatment of relapsed/refractory (r/r) diffuse large B-cell lymphoma (DLBCL). This is based on the early clinical results of JCAR017 obtained from DLBCL patients. Data from this study was presented at the 58th American Society of Hematology Annual Meeting.

JCAR017 uses a defined CD4:CD8 cell composition and 4-1BB as the costimulatory domain, which differentiates it from other CD19-directed CAR-T product candidates in clinical development. JCAR017 is currently being tested in a Phase 1 TRANSCEND trial designed to evaluate the safety and pharmacokinetics of this cell therapy in NHL patients.

In 20 efficacy-evaluable patients treated at dose level 1 (5 x 107 cells), single-dose schedule, the overall response was 16/20 (80%) and complete response (CR) was 12/20 (60%) patients; at dose level 2 (1 x 108 cells), 2/2 (100%) patients evaluable for efficacy had a complete response. In 22 safety-evaluable patients treated at dose level 1, single-dose schedule, no severe cytokine release syndrome was observed; grade 3-4 neurotoxicity was observed in 3/22 (14%) patients, all of whom received the steroid dexamethasone for neurotoxicity. A single patient received tocilizumab for early-onset grade 2 CRS. The most frequently reported treatment-emergent adverse events were neutropenia (100%), decreased appetite (36%) and fatigue (32%).

The TRANSCEND trial continues, enrolling more patients at dose levels 1 and 2. Juno intends to initiate a pivotal trial in the USA in patients with r/r DLBCL in 2017. JCAR017 is also being studied in a Phase 2 study in children with r/r acute lymphoblastic leukemia.

Juno and Celgene started a collaboration in 2015, under which the two companies will leverage T-cell therapeutic strategies to develop

treatments for patients with cancer and autoimmune diseases with an initial focus on CAR and TCR technologies. In April 2016, Celgene exercised its option to develop and commercialize the Juno CD19 program outside North America and China.

Dr Mark J Gilbert, Juno's CMO, commented: "The Breakthrough Therapy designation from the FDA and PRIME eligibility from EMA for JCAR017 highlight the need for new treatment options for patients with DLBCL, particularly for the significant number of patients who do not respond to initial therapy or with relapsed disease. Early data with JCAR017 in a range of B-cell malignancies has been encouraging and we look forward to initiating a pivotal trial in patients with relapsed or refractory DLBCL in the USA in 2017."

Juno Therapeutics' announcement of encouraging preliminary clinical data from its multi-center Phase 1 trial of JCAR017 in non-Hodgkin lymphoma provides some positive news after a difficult year for the company. JCAR017 is a CAR-T treatment that is differentiated from other CD 19-directed CAR-T products in development by using a defined CD4:CD8 cell composition and 4-1BB as the co-stimulatory domain. Efficacy data appear impressive, with a 60% complete response rate at the lower dose level studied, and the safety profile shows manageable toxicities. The news gives the company a new platform to build on, after the disappointment earlier in 2016 of its JCAR015 ROCKET clinical trial in patients with relapsed or refractory B-cell acute lymphoblastic leukemia, which saw several patient deaths, an FDA clinical hold (later removed) and eventual voluntary discontinuation of the program. - Richard Philipson

EDITAS LICENSES NEW TECHNOLOGY AND EXPANDS CRISPR CAPABILITIES

Editas Medicine, a Cambridge, MA-based genome editing company, has entered exclusive license agreements with six world leading research institutes for advancing CRISPR technology. This news has come after some of the most prominent players in the gene editing field have created an IP-sharing alliance on their CRISPR-Cas9 technology, omitting Editas.

The global licensing agreements include intellectual property owned by the Broad Institute of MIT and Harvard (Broad Institute), Harvard University, Massachusetts Institute of Technology (MIT), Wageningen University (The Netherlands), the University of Iowa and the University of Tokyo for the new CRISPR genome editing system known as Cpf1, advanced forms of Cas9, and additional Cas9-based genome editing technologies. This new license could give Editas an advantage in protecting their work just as they are planning to make the big leap into the clinic.

DOI: 10.18609/cgti.2016.078

Under the terms of the combined licenses, Editas will make an upfront payment of $6.25 million and issue a promissory note totaling $10 million that can be settled in stock or cash over a predefined period. The company will also make additional payments upon reaching goals and targets related to research and development, commercialization and market capitalization, and will pay royalties on products based on these technologies.

The Cpf1 gene editing system was developed by a team led by synthetic biologist Dr Feng Zhang of the Broad Institute. This system reportedly is more versatile than Cas9, in that Cpf1 requires only one RNA molecule to replace a DNA sequence rather than two as in Cas9.

Katrine Bosley, CEO of Editas, commented: "We are delighted to expand our global CRISPR genome editing leadership and to build on the ground-breaking work of these important academic institutions to develop both the new genome editing system Cpf1 and advanced forms of Cas9."

KITE COLLABORATES WITH VITRUVIAN NETWORKS TO BUILD LOGISTICS SOFTWARE

Kite Pharma has entered a strategic partnership with San Francisco-based Vitruvian Networks to develop a logistics and data analytics software solution to support the commercial availability of engineered T-cell therapies. This platform is intended for patients, physicians and treatment centers to enable commercial-scale ordering, logistics, monitoring and delivery of autologous cell therapies if they are FDA-approved.

Vitruvian Networks, co-founded by GE Ventures and the Mayo Clinic, is a software and analytics platform company formed to address key challenges in the commercialization and delivery of cell and gene therapies.

Under the terms of the agreement, both parties will contribute resources and expertise to the collaboration. The partnership will bring together Kite's expertise in clinical development, manufacturing, supply chain and commercial leadership in engineered T-cell therapy and Vitruvian's hybrid expertise in building cloud-based software and data analytics solutions in cell and gene therapy manufacturing and delivery settings. Further terms of the agreement were not disclosed.

Tim Moore, Executive Vice President of Technical Operations for Kite, commented: "Kite's technology and services, which will be known as Kite Konnect™, will directly shape the overall experience of patients, physicians and treatment centers as engineered T-cell therapies potentially become available commercially. Our strategic partnership with Vitruvian is a key component of our overall technology strategy and builds on our research collaboration with GE Global Research to automate manufacturing of engineered T-cell therapies."

BLUEBIRD BIO SIGNS MANUFACTURING AGREEMENT WITH APCETH BIOPHARMA

bluebird bio, a clinical-stage company specializing in developing gene therapies for severe genetic diseases, has announced that it has entered a strategic manufacturing agreement with Germany-based apceth Biopharma for the commercial production of two of bluebird's gene therapy products in Europe.

These products include Lenti-D™ and LentiGlobin™ developed for the treatment of cerebral adrenoleukodystropy and transfusion-dependent β-thalassemia, respectively.

apceth Biopharma is a clinical-stage, contract development and manufacturing organization specialized in the development of engineered mesenchymal stem cell therapeutics and cell-based gene therapies.

Under the terms of this multi-year agreement, apceth Biopharma will conduct the clinical manufacturing, process validation activities and commercial manufacturing of the two bluebird products to support the treatment of patients in Europe. bluebird will avail dedicated production suites within apceth Biopharma's state-of-the-art GMP facility at Munich.

Nick Leschly, the chief of bluebird, commented: "We are committed to investing in the capabilities and infrastructure necessary to support commercialization both in the USA and Europe. By partnering with multiple organizations, including our valued partner apceth Biopharma, we are able to develop integrated capabilities in manufacturing that can position us to effectively bring our future commercial products to patients in need."

ADAPTIMMUNE AND BELLICUM PHARMA TO COLLABORATE FOR T CELL THERAPIES

Adaptimmune Therapeutics has entered into a staged collaboration with Oxford, UK-based Bellicum Pharmaceuticals to evaluate, develop and commercialize next-generation T cell therapies.

Adaptimmune is a clinical-stage biopharmaceutical company specialized in developing cancer immunotherapy products based on its Specific Peptide Enhanced Affinity Receptor (SPEAR) T cell platform. Bellicum, using its proprietary chemical induction of dimerization (CID) technology platform, is focusing on developing next-generation, controllable cellular immunotherapies for cancers and orphan inherited blood disorders.

Under the terms of the agreement, the companies will evaluate Bellicum's GoTCR technology (inducible MyD88/CD40 co-stimulation or iMC) with Adaptimmune's

DOI: 10.18609/cgti.2016.078

affinity-optimized SPEAR® T cells for the potential to create enhanced TCR product candidates. Depending on results from the preclinical proof-of-concept phase, the companies expect to progress to a two-target co-development and co-commercialization phase.

James Noble, Adaptimmune's CEO commented: "As we advance our deep pipeline of second- and third-generation SPEAR T cell therapies, we are excited by the potential of Bellicum's iMC switch to complement the activity of our affinity enhanced T cell therapies, as part of our continuing initiative to assess novel cell therapy enhancement technologies. This is an innovative field that requires broad, industry-wide collaborations, such as our relationship with Bellicum and its strong leadership position in switch technology."

Adaptimmune and Bellicum Partnership

Adaptimmune and Bellicum have entered a collaboration to complete preclinical proof-of-concept work on TCR technologies that combine Adaptimmune's affinity-enhanced SPEAR platform and Bellicum's GoTCR platform. The GoTCR platform incorporates an inducible switch wherein full activation of the targeting construct requires the presence of both a cancer antigen and the small molecule rimiducid. Using this approach the therapeutic remains partially active in the absence of the cancer antigen providing rimiducid is still present in the patient, which ensures ongoing surveillance following eradication of cancer cells. Pending positive preclinical data the companies will move towards a multi-target co-development program. – *Mark Curtis*

CALIMMUNE EXPANDS ITS GENE THERAPY PIPELINE TO TREAT HEMOGLOBINOPATHIES

Calimmune, a US-based clinical-stage gene therapy company has announced a license agreement with Cincinnati Children's Hospital Medical Center to develop and commercialize gene therapy for sickle cell disease and beta thalassemia.

Through this collaboration, which combines Calimmune's Select+™ technology with Cincinnati Children's proprietary lentiviral gene therapy construct, the company intends to create permanent treatment solutions for hemoglobinopathy patients who are facing shortened life expectancy and reduced quality of life.

Calimmune's Select+™ platform is aimed to drive selection of the genetically modified stem cells in the patient's body, to improve engraftment and lower toxicity. The procedure involves introduction of the gamma-globin gene into the patient's own hematopoietic stem

cells (HSCs) using a self-inactivating lentiviral vector. Following this, Calimmune's Select+™ technology is used to positively select for the modified HSCs, thus increasing the population of modified cells versus unmodified cells in the patient's system.

Dr Salim Yazji, Calimmune's CMO commented: "The combination of Cincinnati Children's proprietary lentiviral construct with Calimmune's Select+ technology is a powerful innovative step in the fight against debilitating hematologic conditions such as sickle cell disease and beta thalassemia. We are applying our unique experience in *ex vivo* lentiviral vector gene therapy to make treatments for hemoglobinopathy more effective, less toxic and ultimately more accessible to the patients that need them."

PLURISTEM SIGNS AGREEMENT WITH SOSEI CVC TO COMMERCIALIZE PLX-PAD IN JAPAN

Pluristem Therapeutics, an Israel-based developer of placenta-based cell therapy products has announced the signing of a binding term agreement with Corporate Venture Capital Ltd (Subsidiary of Sosei Group Corporation, a Tokyo Stock Exchange Mothers listed company) for the establishment of a new Japanese corporation (NewCo) aimed at the clinical development and commercialization of Pluristem's PLX-PAD cell therapy product in Japan.

Under the terms of the agreement, Pluristem will own 35% of NewCo in return for its contribution of a perpetual license to commercialize PLX-PAD for critical limb ischemia (CLI) in Japan. All rights related to PLX-PAD will be owned by Pluristem. Sosei CVC's investment fund, Sosei RMF1, together with additional Japanese investors, will raise and invest approximately $11 million, equivalent to approximately ¥1.3 billion, in return for ownership of 65% of NewCo.

The first indication to be developed by NewCo will be CLI. Japan's regulatory agency has already agreed on the study design of a clinical trial in CLI with 75 patients for potential conditional marketing approval under an accelerated pathway. Future marketing activities are planned to be undertaken by NewCo. The parties plan to enter a definitive agreement by March 2017.

Zami Aberman, Pluristem's Chairman and CEO, commented: "We are pleased to partner with Sosei CVC to commercialize PLX-PAD in Japan. The development of our CLI program through the accelerated regulatory pathway could allow a more rapid entrance into the sizeable Japanese market, as has been our strategy. Our cooperation with Sosei CVC also creates the potential to develop additional indications in this market, by drawing on our robust portfolio of cell therapy product candidates in development."

DOI: 10.18609/cgti.2016.078

KIADIS PHARMA NAMES ARTHUR LAHR AS NEW COO AND CEO DESIGNATE

Kiadis Pharma has announced the appointment of Arthur Lahr as its COO and CEO designate. As the company is advancing into a late-stage clinical/pre-commercialization phase, Dr Manfred Rüdiger, Kiadis' current CEO will hand over his responsibilities to Mr Lahr on April 1 2017 as part of a planned and thoroughly executed succession plan.

Mr Lahr has significant experience in the healthcare sector and joins Kiadis from Crucell. He was the Chief Strategy Officer and member of the management committee at Crucell from 2001 until its acquisition by Johnson & Johnson for $2.4 billion in 2011. Prior to that, he was a consultant at McKinsey & Company between 1994 and 2001.

BLUEBIRD BIO EXPANDS ITS LEADERSHIP TEAM

bluebird bio has announced the appointment of Susanna High as its new CTO and Andrew Obenshain as its Senior Vice President and Head of Europe.

Ms High has 20 years of strategic and operational experience in the biopharmaceutical industry. Most recently, she worked at Alnylam Pharmaceuticals where she held various rolves involving company strategy, business planning and broader organizational capability building initiatives. Prior to that, she worked at Millennium Pharmaceuticals (now Takeda Oncology).

Before joining bluebird bio, Mr Obenshain served as General Manager at Shire in France. Prior to Shire, he worked at Genzyme and Sanofi, holding responsibilities in business development, marketing and global commercial operations.

Written by Applonia Rose, Commissioning Editor, Cell and Gene Therapy Insights