Commercial insight: cell and gene therapy

JAN 2017

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

GENE THERAPY
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GENE THERAPY: This month sees several companies advancing their programs by achieving important regulatory milestones, including Rare Pediatric Disease status for Lysogene's AAV-based treatment for GM1 gangliosidosis, Orphan Drug Designation in Europe for Abeona's AAV-based treatment for San Filippo B, and Fast Track Designation in the USA for Fibrocell's autologous, fibroblast-based gene therapy treatment for dystrophic epidermolysis bullosa. Spark Therapeutics continues to release positive news on an almost monthly basis, with the announcement that a $15 million milestone payment has been triggered, and Sarepta Therapeutics builds on the recent approval of its exon-skipping therapy for Duchenne muscular dystrophy with the announcement of a research collaboration with Nationwide Children's Hospital, where they will work together on their microdystrophin program, as well as another form of gene therapy.

CELL THERAPY: It was a busy start to 2017 with multiple new immunotherapy products en route to the clinic. Kite submitted an IND for KITE-718, a TCR technology

targeted to MAGE antigens that will be deployed for multiple solid tumor indications. Adaptimmune had an IND accepted for a TCR, also targeted to MAGE. On this front GSK also nominated its second target from Adaptimmune (PRAME) under its collaboration agreement signed back in 2014. Adaptimmune will bring the technology to IND readiness, after which it will be handed off to GSK to complete development. Cellectis submitted an IND for a gene-edited CAR product (UCART123) that will be targeted to AML and BPCDN, the first IND filing for an off-the-shelf T-cell product in the USA. Cellectis' product wasn't the only first in the USA though, NantKwest made headlines delivering the first off-the-shelf, engineered NK cell product into the clinic (haNK), which, like Kite and Adaptimmune's products, will be targeted to solid tumors. It's clear the race this year will be to demonstrate efficacy data in solid tumors, rather than liquid.

TOCAGEN EXTENDS GENE THERAPY TRIAL TO SOUTH KOREA

Tocagen, a clinical-stage company developing cancer-selective viral gene therapy, has announced that Toca 5, its Phase 2/3 clinical trial designed to treat high-grade glioma (HGG), is enrolling patients in South Korea. The trial is currently ongoing in the USA, Canada and Israel.

HGGs are among the most common and aggressive primary brain tumors. The two most common forms of HGGs are glioblastoma (GBM) and anaplastic astrocytoma. In 2016, approximately 160,000 patients worldwide are thought to have been diagnosed with HGG. With current standard of care, newly diagnosed GBM patients have a median survival of approximately 16 months.

Toca 5 is an investigational therapy that combines Tocagen's Toca 511 (vocimagene amiretrorepvec) and Toca FC (extended-release 5-fluorocytosine). Toca 511 is a retroviral replicating vector that delivers a yeast cytosine deaminase selectively to cancer cells, which converts subsequently administered investigational prodrug (Toca FC) from 5-fluorocytosine to the antimetabolite 5-fluorouracil, a potent anticancer drug. The study is designed to evaluate Toca 5 in patients with first or second recurrence of glioblastoma or anaplastic astrocytoma who are undergoing resection.

A total of 126 patients were treated in Tocagen's Phase 1 ascending-dose studies. Results obtained from 45 subjects with recurrent or progressive HGG were published in 2016 in the journal *Science Translational Medicine*, which showed significant improvement in the survival rate and clinical benefit rate after administration of Toca 5. Toca 511 and Toca FC showed a favorable safety profile and was well tolerated by patients.

Dr Do Hyun Nam of Sungkyunkwan University School of Medicine, which enrolled the first patient in South Korea, commented: "Brain tumors are among the deadliest of all cancers and there are very few treatment options available. Data

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from Phase 1 studies of this investigational agent showed very promising safety, survival and durable tumor response data so we are excited to continue evaluation of this therapy in the Toca 5 trial."

LYSOGENE'S GENE THERAPY RECEIVES RARE PEDIATRIC DISEASE STATUS

The US FDA has granted Rare Pediatric Disease designation to Lysogene's gene therapy candidate, LYS-GM101, developed for the treatment of GM1 gangliosidosis (GM1), a severe neurodegenerative disease. Through this Rare Pediatric Disease status, Lysogene has become eligible for a Rare Pediatric Disease Priority Review Voucher from the FDA upon approval of LYS-GM101.

GM1 is a lysosomal storage disorder caused by the deficiency of β-galactosidase enzyme, resulting in the accumulation of GM1 gangliosides and related glycoconjugates in the lysosomes. It leads to lysosomal swelling and organ dysfunction. The disease is lethal in the infantile and juvenile forms. Lysogene's LYS-GM101 is an adeno-associated virus vector containing the human gene for the β-galactosidase enzyme.

Lysogene is a clinical-stage biotechnology company specialized in the development of adeno-associated virus (AAV)-mediated gene therapy for central nervous system disorders. Currently, Lysogene is developing IND-supporting preclinical studies for LYS-GM101 in collaboration with the University of Massachusetts Medical School and Auburn University.

Karen Aiach, Founder and CEO of Lysogene, commented: "This Rare Pediatric Disease Designation for LYS-GM101 is Lysogene's second designation after the LYS-SAF302 designation for the treatment of MPS IIIA. We look forward to continuing to advance this product candidate in our upcoming Phase I/II clinical trial (LYS-GM101)."

KITE TO INITIATE A T-CELL THERAPY TRIAL FOR SOLID TUMORS

Kite Pharma, a California-based clinical-stage biopharmaceutical company, has announced that it has submitted an Investigational New Drug (IND) application to the US Food and Drug Administration (FDA) to initiate a Phase 1 trial of KITE-718, an engineered T-cell therapy that targets MAGE A3 and MAGE A6 on solid tumors.

MAGE A proteins are testis-specific E3 ubiquitin ligase components whose expression is upregulated in many cancers. MAGE A3 and A6 are frequently overexpressed in common solid tumors including bladder, esophageal, head and neck, lung and ovarian cancers.

Kite's KITE-718 trial is designed to assess the safety and anti-tumor effect of KITE-718 on these solid tumors. This investigational therapy has the potential to recognize MAGE A3 and MAGE A6

fragments on tumors and kill tumor cells through activation of the immune system.

KITE-718 is built on the proof of concept data obtained from the National Cancer Institute's (NCI) MAGE A3 TCR program (NCT02111850), where engineered T cells were used for the treatment of metastatic cancers, by targeting the MAGE A3 proteins. No off-target toxicity was observed in the NCI study, and evidence of tumor regression was seen in patients with multiple types of solid tumors. Kite has further optimized the manufacturing process through advanced technologies and next-generation cell manufacturing conditions.

Dr David Chang, Kite's CMO, commented: "Submission of this IND is an important milestone for our solid tumor strategy utilizing engineered T-cell therapy based on both TCR and CAR platform technology. TCRs have the potential to access a broad spectrum of tumor targets and we have incorporated our next-generation cell manufacturing technologies into KITE-718 to exploit targets naturally expressed in common solid tumors for which there is a great unmet medical need."

ABEONA'S GENE THERAPY CANDIDATE RECEIVES EMA'S ORPHAN DRUG DESIGNATION

Abeona Therapeutics, a US-based clinical-stage company, has announced that the European Medicines Agency (EMA) has granted Orphan Drug Designation to its gene therapy candidate, ABO-101, designed for the treatment of children with Sanfilippo Syndrome type B (Mucopolysaccharidosis Type IIIB or MPS IIIB).

MPS IIIB is a rare autosomal recessive disease that causes neurocognitive decline, speech loss, loss of mobility and premature death in children. The disease is caused by mutations in a gene that codes for the enzyme, N-acetyl-α-D-glucosaminidase (Naglu). Deficiency of Naglu causes the accumulation of heparan sulfate in cells, particularly of the central nervous system.

ABO-101, Abeona's first-in-human gene therapy uses an adeno-associated viral-based gene therapy approach for MPS IIIB and involves a one-time delivery of a normal copy of the *Naglu* gene to cells of the central nervous system and peripheral organs.

Preclinical studies have shown that a single dose of ABO-101 induced cells in the central nervous system and peripheral organs to produce the missing enzyme and remove the associated pathology in cells. *In vivo* efficacy studies have also demonstrated functional benefits in animal models that persisted for months following treatment. One time delivery of ABO-101 significantly restored normal cell and organ function, corrected cognitive defects, increased neuromuscular function and normalized the lifespan of animals with MPSIIIB after treatment.

ABO-101 has been granted Orphan Product Designation and Rare Pediatric Disease Designation by the US FDA and received the Rare Pediatric Disease Designation. The

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FDA has allowed the Investigational New Drug (IND) for a Phase 1/2 clinical trial, and enrollments are anticipated to begin in the second quarter of 2017.

Timothy J Miller, Abeona's President and CEO, commented: "This designation builds on our commercial portfolio of AAV gene therapies that have received FDA and EMA orphan drug designations, which is an important validation of the scientific and clinical translation of these products for severely underserved patient populations. Accomplishing the designation would not have been possible without the contributions of Nationwide Children's Hospital researchers Drs Doug McCarty and Haiyan Fu, the Stop Sanfilippo Fundacion, Fundacion Sanfilippo B, Red Sanfilippo Fundacion, the Sanfilippo Children's Research Foundation, Ben's Dream, the Sanfilippo Medical Research Foundation, Team Sanfilippo and the National MPS Society USA."

In additional news this month, Abeona's ABO-201 gene therapy candidate has also been granted EMA's Orphan Drug Designation. ABO-201 is an AAV-based single intravenous gene therapy program for juvenile Batten disease, a fatal lysosomal storage disease of the nervous system caused by autosomal recessive mutations in the *CLN3* gene.

Abeona Therapeutics continues to build momentum with its gene therapy candidate ABO-101 for the lysosomal storage disease San Filippo B, adding Orphan Drug Designation from the EMA to Orphan Product and Rare Pediatric Disease Designations already awarded by the FDA. The AAV-based one-off gene therapy differs from the approach taken by companies such as Alexion and Shire, who have focused instead on developing enzyme replacement therapies to be given on an ongoing basis. The company has also announced that it is only weeks away from enrolling the first patients in a clinical trial of ABO-101, a decision that comes after its co-lead program, ABO-102 for San Filippo A, showed promising initial data in a Phase 1/2 trial. – **Richard Philipson**

CELYAD INITIATES ITS NKR-2 CAR-T TRIAL IN BELGIUM

Celyad, a Belgium-based pharmaceutical company specialized in the development of engineered cell therapies, has announced registration of the first patient in Belgium, for its THINK trial, designed to evaluate CAR T-cells that recognize NKG2D-ligands on the surface of cancer cells.

Blood from this first colorectal cancer patient was collected and the processing has been initiated at Celyad's manufacturing facility at Mont-Saint-Guibert. The resulting CAR-T NKR-2 cells will be infused to the patient this month at a dose of 3 x 10^8 cells.

The THINK (Therapeutic Immunotherapy with NKR-2) trial is a multi-center, dose-escalation, Phase 1b study designed to investigate the safety and clinical activity of administering multiple doses of autologous NKR-2 CAR T-cells

in patients with seven refractory cancers including five solid tumors (colorectal, ovarian, bladder, triple-negative breast and pancreatic cancers) and two hematological tumors (acute myeloid leukemia and multiple myeloma). These seven indications were selected on the basis of preliminary evidences obtained from Celyad's recently completed Phase 1 trial of NKR-2 T cells in patients with acute myeloid leukemia or multiple myeloma.

This trial consists of two stages: a dose escalation stage and an extension stage. The dose escalation will enrol up to 24 patients and will be conducted in parallel in the solid and liquid cancer groups. In this phase, three doses of NKR-2 T cells will be tested and patients will receive three successive administrations of each specified dose, 2 weeks apart. The extension phase will evaluate in parallel each tumor independently and will enroll 86 additional patients.

Dr Frédéric Lehmann, VP Clinical Development and Medical Affairs at Celyad, commented: This is an important moment for Celyad. The THINK trial aims to demonstrate that CAR-T NKR-2 cells can deeply transform the way we treat cancer patients. The team keeps on showing its awe-inspiring ability to deliver in research and development, and the company has now reached a cardinal inflection point to emerge as a key player in the CAR-T space".

FDA GRANTS FAST TRACK DESIGNATION TO FIBROCELL'S FCX-007 FOR THE TREATMENT OF EPIDERMOLYSIS BULLOSA

Fibrocell, an autologous cell and gene therapy company, has received Fast Track designation from the FDA for their product FCX-007, developed for the treatment of recessive dystrophic epidermolysis bullosa (RDEB).

RDEB is a devastating, and often fatal, inherited blistering disorder of the skin caused by mutations in the *COL7A1* gene encoding type VII collagen. FCX-007, developed in collaboration with Intrexon Corporation, is an autologous fibroblast cell genetically modified to express collagen VII at the wound site of patients. It offers the potential to address the underlying cause of the disease by providing high levels of collagen VII directly to the affected areas while avoiding systemic distribution.

Fast Track designation is granted to facilitate development and expedite review of new therapies that address unmet medical needs. It allows more frequent meetings with the FDA to discuss the drug's development plan, eligibility for Priority Review if relevant criteria are met, and opportunity for Rolling Review, which allows Fibrocell to submit completed sections of its Biologics License Application (BLA) to the FDA, rather than waiting until every section of the BLA is completed before the entire application can be reviewed. FCX-007 was previously granted Orphan Designation and Rare Pediatric Disease Designation by the FDA for the treatment of RDEB.

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The announcement of the award of Fast Track Designation to Fibrocell's gene therapy FCX-007 for dystrophic epidermolysis bullosa (DEB) is encouraging news for patients and their families. DEB is a devastating condition causing widespread skin blistering, limb deformities, joint contractures and increased risk of skin cancer. Fibrocell's technology uses autologous fibroblasts, expanded ex vivo and transfected using a third generation, self-inactivating lentivirus, which transfects cells with the COL7A1 gene; the modified fibroblasts are then administered locally to promote tissue repair through secretion of COL7. There are currently no approved therapies for DEB, although several topical and systemic therapies are in clinical trials, including other gene therapies targeting fibroblasts. – Richard Philipson

ASTERIAS' STEM CELL TRIAL SHOWS POSITIVE EFFICACY DATA IN SPINAL CORD INJURY PATIENTS

Asterias Biotherapeutics, a California-based clinical-stage biotechnology company, has announced positive interim efficacy data from its ongoing Phase 1/2a SCiSTAR trial designed to evaluate the activity of escalating doses of AST-OPC1 (oligodendrocyte progenitor cells) in patients with complete cervical spinal cord injury.

The trial included three cohorts: an initial cohort of three patients who received 2 million AST-OPC1 cells and a second cohort of six patients who were dosed with 10 million AST-OPC1 cells. The third cohort of 5–8 patients will be administered with the highest dose of 20 million cells.

Five out of six patients in the second cohort completed their 6-month follow-up and three out of 6 patients completed their 9-month follow-up. Patient improvements were measured by the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) neurological classification scale, which is widely used to quantify functional status of patients with spinal cord injuries.

Results showed that all five evaluable patients displayed meaningful improvements in their ability to use their arms, hands and fingers at 6 months and 9 months following AST-OPC1 administration. All five patients who completed 6 months follow-up achieved at least one motor level improvement, two of five achieved two motor levels on at least one side and one of five patients achieved two motor level improvement on both sides. Results also showed that AST-OPC1 was well tolerated by patients with no serious adverse events reported.

According to the study's lead investigator Dr Richard Fessler of Rush University Medical Center, the results obtained are promising as recovery of upper extremity motor function is critically important to patients with complete cervical spinal cord injuries.

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 August 2016, the company had received safety clearance from its Data Monitoring Committee to pursue dosing of a third cohort of subjects.

Steve Cartt, CEO of Asterias, commented: "These results to date are quite encouraging, and we look forward to initiating discussions with the FDA in mid-2017 to begin to determine the most appropriate clinical and regulatory path forward for this innovative therapy. In addition, we anticipate reporting 12-month efficacy and safety data for this cohort, as well as 6-month efficacy and safety data for the currently-enrolling AIS-A 20 million cell and AIS-B 10 million cell cohorts, during the third quarter of 2017."

Following the news, shares in Asterias increased 4% in premarket trading, but then fell when trading began by more than 7% yesterday morning.

CELLECTIS INTRODUCES A SAFETY FACTOR IN ITS CAR DESIGN

Cellectis, a biopharmaceutical company specialized in developing immunotherapies based on gene edited CAR-T cells (UCART), has announced the development of a novel approach to introduce an additional level of safety to its CAR-T technology. The design has an integrated oxygen sensor that responds to oxygen concentration in the microenvironment to manipulate the CAR-T cell response.

A microenvironment with low oxygen concentration is one of the hallmarks of solid tumors. Through the implementation of oxygen sensor in the CAR design, the resulting CAR-T cells will have the possibility to auto-regulate (switch on or off) their functions in low oxygen (hypoxic) environments. This *in vitro* proof of concept study is published in *Scientific Reports*.

Results showed that this self-decision making CAR-T cells minimized 'on-target/off-tumor' effects and possessed the key feature of being able to return to an off state in the absence of the inducing signal (hypoxia), a characteristic that is of prime interest to protect healthy tissues distant from the tumor site. Cellectis is planning to conduct additional *in vivo* studies to fully evaluate the therapeutic potential of this approach.

In additional news this month, the company has announced the submission of an IND application to the FDA requesting approval to initiate a Phase 1 clinical trial of UCART123 in patients with acute myeloid leukemia (AML) and blastic plasmacytoid dendritic cell neoplasm (BPDCN). This is the first IND filing for human clinical applications of a gene edited allogeneic off-the-shelf product candidate in the USA.

Following regulatory clearance, Cellectis plans to initiate the trial in the first half of 2017. UCART123 is a gene edited T-cell investigational drug that targets CD123, an antigen expressed on the surface of leukemic cells in AML and other tumoral cells in BPDCN.

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CELLECTIS CONTINUING TO PUSH INNOVATION IN CAR PRODUCTS

Cellectis is pushing the envelope in designer cells for immunotherapy. The company recently published a paper describing a new architecture that gives CAR products the ability to auto-regulate following administration to the patient. One of the ongoing safety issues with CAR products are on-target/off-tumor effects, which lead to toxicity. The new CAR design devised by Cellectis and its collaborators takes advantage of the hypoxic environment that is a hallmark of solid tumors. The architecture includes an integrated microenvironment sensor that leads to activation of the CAR in low oxygen environments, which ultimately may improve the safety profile of CAR products. Importantly, the designer CARs rapidly return to an 'off' state once normal oxygen levels return. – Mark Curtis

NANTKWEST TO INITIATE A FIRST-IN-HUMAN NK CELL THERAPY TRIAL FOR CANCERS

NantKwest has announced that the FDA has approved its IND application to initiate a Phase 1 trial of haNK, an engineered natural killer (NK) cell therapy to treat solid tumors.

The haNK cell therapy platform is an allogeneic, off-the-shelf therapy that exploits NK cells' innate ability to rapidly identify and destroy cells under stress, such as cancer cells, and improves anti-tumor responses via antibody-dependent cell-mediated cytotoxicity. To achieve this, haNK cells have been engineered to express IL-2 and the high-affinity variant of the CD16 receptor.

This Phase 1 study is designed to determine the safety of haNK cell monotherapy administered intravenously once per week in up to 16 patients with metastatic or locally advanced solid tumors. Other objectives of the trial include determination of objective response rate, progression-free survival, overall survival and any correlations between tumor molecular profiles and patient outcomes.

Preclinical studies have demonstrated the potential of haNK cells to destroy tumor cells when added to a variety of therapeutic antibodies. The company intends to initiate this first-in-human clinical study promptly to provide the necessary safety data to rapidly transition to haNK-antibody combination trials.

Dr Patrick Soon-Shiong, Chairman and CEO of NantKwest, commented: "We are thrilled to have received notification from the FDA that our first haNK cell therapy program has been authorized to proceed into Phase I clinical trials and are focused on moving swiftly to begin this study. The FDA's authorization to initiate this clinical trial achieves a significant milestone for NantKwest as we begin clinical investigation of the use of haNK cell therapy for the treatment of cancer in a wide range of cancer types."

STEMCELL TECHNOLOGIES OPENS NEW FACILITY IN CAMBRIDGE, UK

STEMCELL Technologies, a Canadian biotechnology company, has recently opened their new office and laboratories in Cambridge, UK.

STEMCELL Technologies is specialized in developing reagents and tools to support life sciences research, regenerative medicine and cell therapy. With over 2000 cell biology research tools, the company supports the advancement of scientific research around the world. Cambridge is a leading global hub for stem cell research and with the opening of this new facility the company intends to build its portfolio and advance as a major service provider in the industry.

The new 18,000 square foot facility is situated in the Cambridge research park and it has now consolidated existing UK staff into the facility, which at full capacity will house a Research and Development group, Sales, Marketing and other support staff. The facility's major focus is to develop a state-of-the-art Education and Teaching Lab, to offer training courses and workshops, to help researchers develop expertise in cell culture protocols and techniques.

Dr Allen Eaves, CEO and President of STEMCELL Technologies, commented: "STEMCELL is committed to driving the advancement of science by offering the highest quality products and services to support scientists with their research. We are thrilled to be officially opening our new Cambridge office, including our Research and Development labs and Education Centre. STEMCELL has seen fantastic growth, and this facility will take us to the next level in supporting medical sciences research globally, as well as open our doors to the incredible biomedical expertise in the UK and Europe."

SAREPTA THERAPEUTICS COLLABORATES WITH NATIONWIDE CHILDREN'S HOSPITAL

Sarepta Therapeutics, a commercial-stage biopharmaceutical company specialized in the development of RNA-targeted therapeutics for the treatment of rare neuromuscular diseases, has announced that it has entered a research and option agreement with Nationwide Children's Hospital on their microdystrophin gene therapy program.

Drs Jerry Mendell and Louise Rodino-Klapac are the lead principal investigators of the program. The Phase 1/2a trial is expected to initiate in late 2017 and will be conducted at Nationwide Children's Hospital.

Parent Project Muscular Dystrophy (PPMD) has committed 2.2 million dollars to the trial, with support from additional Duchenne foundations and families. Sarepta has committed to the trial through a separate research agreement with

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Nationwide Children's Hospital, and has an exclusive option to license the program. PPMD's grant provided incentive for Sarepta to help expand and accelerate this opportunity.

Sarepta is primarily focused on rapidly advancing the development of its potentially disease-modifying DMD drug candidates.

Edward Kaye, Sarepta's CEO, commented: "Given the complexities of Duchenne muscular dystrophy, we know that it is going to require multiple treatment approaches. With that goal in mind, we are excited to support clinical development for Nationwide's gene therapy program with the goal to help all boys with DMD."

KITE PARTNERS WITH DAIICHI SANKYO TO COMMERCIALIZE CAR-T CELL THERAPY IN JAPAN

Kite Pharma has announced that it has entered a strategic collaboration with Daiichi Sankyo, to develop and commercialize its T-cell therapy axicabtagene ciloleucel in Japan.

Axicabtagene ciloleucel is the US Adopted Name (USAN) for KTE-C19, Kite's lead product candidate developed for the treatment of relapsed/refractory aggressive B-cell non-Hodgkin lymphoma (NHL).

Under the terms of the agreement, Daiichi Sankyo will develop and commercialize axicabtagene ciloleucel in Japan. Kite will receive an upfront fee of $50 million from Daiichi Sankyo and is also eligible for additional payments totaling up to $200 million upon achievement of development and commercial milestones. Kite is also entitled to receive sales royalties. Kite will retain all development and commercialization rights outside of Japan.

As part of the agreement, Kite will provide certain technical transfer services to Daiichi Sankyo. In the future, Daiichi Sankyo will also commercialize additional Kite product candidates in Japan, including KITE-718, Kite's T-cell receptor product candidate. Upfront and milestone payments for each additional product candidate could equal up to $200 million plus sales royalties.

In December 2016, Kite had announced that it 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 NHL. The company expects to complete its BLA submission by early 2017. If BLA is approved, the company plans to commercially launch KTE-C19 in 2017 and also aims for a regulatory submission to the EMA.

KTE-C19 was granted Breakthrough Therapy Designation by the FDA in 2015 for the treatment of three subtypes of aggressive NHL: chemorefractory diffuse large B-cell lymphoma, transformed follicular lymphoma and primary mediastinal B-cell lymphoma. It also gained access to the EMA's Priority Medicines (PRIME) support for the treatment of DLBCL in 2016.

Arie Belldegrun, Kite's CEO, commented: "We are thrilled to

partner with Daiichi Sankyo, a market leader in Japan who shares our vision for engineered T-cell therapy and has strong development capabilities in oncology. We have a strategic roadmap to commercialize axicabtagene ciloleucel globally while focusing Kite's development and commercialization efforts in the USA and Europe. Daiichi Sankyo's commitment to bring autologous T-cell therapy to patients in Japan will complement our strategy and demonstrates the significant value in our pipeline, as well as the commercial potential for autologous T-cell therapy globally."

KITE PUSHING INTO ASIA

Kite Pharma is leaving no stone unturned in its quest to bring axicabtagene ciloleucel to the patient. While it awaits approval in the USA, the company has been aggressively pursuing a commercial strategy in Asia, which includes deals in both China and Japan. In exchange for $50 milliom upfront, and $200 million in future milestone payments, Kite gave Daiichi-Sankyo commercial rights to axicabtagene ciloleucel in Japan. The company also forged a JV with Fosun Pharma for $40 million upfront, development milestones, profit sharing and a royalty, that will see Fosun market axicabtagene ciloleucel, and up to two other product candidates from Kite's pipeline, in China. – Mark Curtis

INTREXON TO ACQUIRE GENVEC TO EXPAND ITS GENE DELIVERY CAPABILITIES

Maryland-based Intrexon has announced that it has entered a definitive agreement to acquire GenVec, a clinical-stage company specialized in developing gene delivery technologies. With this acquisition plan, Intrexon aims to become a major player in the gene therapy industry.

The acquisition will combine GenVec's expertise in adenoviral vectors and cGMP drug product manufacturing with Intrexon's gene transfer capabilities that encompass multiple viral and non-viral platforms. The combined technology is expected to have the potential to create the next generation of adenoviral delivery through the creation of a scalable manufacturing platform utilizing helper-dependent adenovirus, which has a higher payload capacity (>30kb) as compared to that of the current viral delivery methods (4.5–9kb).

GenVec is specialized in adenovector design, testing, scale-up and manufacture. Its AdenoVerse™ technology is currently being tested in various pre-clinical and clinical trials for a wide variety of applications, including cell therapy, regenerative medicine, cancer

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therapeutics, vaccines and antivirals. Through an adenovirus-based vector, Intrexon has already delivered the first clinically validated transcriptional gene switch utilizing the RheoSwitch Therapeutic System® to regulate the expression of interleukin 12, to treat cancer.

Under the terms of the agreement, Intrexon has agreed to pay $7 a share, a price approximately 50% higher than the price GenVec was trading at prior to news of the deal. Intrexon will also give GenVec shareholders half of any milestones and royalties that result from the latter's pact with Novartis over the next 3 years. Consummation of the acquisition is subject to customary closing conditions, including GenVec stockholder approval, and is expected to occur in the second quarter of 2017. Hogan Lovells and Thompson Hine are serving as legal counsels to GenVec and Intrexon, respectively.

Dr Thomas Reed, Intrexon's CEO, commented, "Our acquisition of GenVec will mark our continuing commitment to add gene delivery platforms that complement our multigenic control systems. Intrexon's proficiency in using various viral as well as non-viral transfer techniques to integrate our gene programs affords us the capability to pursue an array of *in vivo* and *ex vivo* gene and cell therapy approaches, and the addition of a helper-dependent adenoviral system with a substantial payload capacity dramatically expands the types of *in vivo* therapeutic programs we can pursue."

GSK NOMINATES A SECOND TARGET UNDER ITS COLLABORATION WITH ADAPTIMMUNE

Adaptimmune, a clinical-stage biopharmaceutical company specialized in developing cancer immunotherapy products based on its Specific Peptide Enhanced Affinity Receptor (SPEAR™) T-cell platform, has announced that GlaxoSmithKline (GSK) has nominated a second target, preferentially expressed antigen in melanoma (PRAME), under the strategic collaboration and licensing agreement between the companies.

Adaptimmune and GSK entered a licensing agreement in 2014 for up to five Adaptimmune programs, the first being the NY-ESO SPEAR® T-cell therapy program. The agreement was subsequently expanded in 2016 to expedite the development of NY-ESO SPEAR T-cell therapy toward registration trials in synovial sarcoma. Following the nomination of PRAME as a second target, Adaptimmune will be responsible for PRAME preclinical development and delivery of the IND package to GSK.

Under the terms of the agreement, Adaptimmune is eligible to receive approximately $300 million solely for the PRAME program, if GSK exercises its option and successfully develops this target in more than one indication. Adaptimmune is also eligible to receive sales milestones and royalties on worldwide net sales.

Helen Tayton-Martin, Adaptimmune's Chief Operating Officer, commented: "The nomination of this next target marks an important step forward for the collaboration. The early clinical results we have seen in synovial sarcoma with our SPEAR T-cell therapy targeting NY-ESO-1 have been promising thus far, and we are accelerating that program toward registration studies. The nomination of PRAME as GSK's second target is further validation of our technology, and our goal is to deliver this IND package as expeditiously as possible."

ADURO BIOTECH TO COLLABORATE WITH MERCK IN THE FIGHT AGAINST GASTRIC CANCER

Aduro Biotech, an international immunotherapy company, has announced that it has entered a clinical collaboration agreement with Merck to evaluate Aduro's CRS-207 immunotherapy in combination with Merck's KEYTRUDA® for the treatment of gastric cancer.

CRS-207 is Aduro's live, attenuated double-deleted *Listeria monocytogenes* strains that have been engineered to express the tumor-associated antigen mesothelin, which is overexpressed in many cancers. The product generates a potent innate immune response and induces tumor-specific T-cell mediated immunity. Merck (known as MSD outside the USA and Canada)'s KEYTRUDA is a humanized monoclonal antibody that blocks the interaction between PD-1 and its ligands, thereby activating T lymphocytes and potentiating antitumor activity. The multicenter Phase 1 study, planned to begin in the first half of the year, will enroll patients with metastatic gastric cancer who have failed at least two prior therapies to receive the combination of CRS-207 and pembrolizumab.

SPARK EARNS $15 MILLION MILESTONE PAYMENT FROM PFIZER

Spark Therapeutics, a gene therapy company, has announced that it has earned a $15 million payment from Pfizer for achieving a pre-specified safety and efficacy development milestone in their ongoing clinical trial for hemophilia B, a rare genetic bleeding disorder.

This 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.

Spark Therapeutics and Pfizer entered into a collaboration in 2014 for the *SPK-FIX* program,

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under which Spark is responsible for conducting all Phase 1/2 studies for any product candidates, while Pfizer holds responsibility for pivotal studies, any regulatory activities and global commercialization of any products that may result from the collaboration. Spark received a $20 million upfront payment then, and a $15 million milestone payment in 2015 for progress with the development program. The company is eligible to receive up to an additional $230 million in aggregate for achieving future development and commercial milestones, as well as royalties calculated as a low-teen percentage of net sales on any potential *SPK-FIX* products.

Jeffrey D Marrazzo, Spark's CEO, commented: "We continue to make strong, tangible progress with our hemophilia pipeline, and achievement of this second milestone marks further advancement in the development of our investigational gene therapy for hemophilia B. We look forward to reporting additional data as we continue to document the clinical experience with SPK-9001."

MARK DUDLEY JOINS ADAPTIMMUNE AS SENIOR VP

Adaptimmune Therapeutics has announced the appointment of Dr Mark E Dudley as its Senior VP of Global Bio-Process and Development.

Dr Dudley, one of the pioneers in the field of immunotherapy manufacturing, has had significant experience in the cell and gene therapy manufacturing sector. Prior to joining Adaptimmune, he was the Director of New Cell Products for Cell and Gene Therapy at Novartis where he was responsible for establishing scalable, GMP compliant production strategies, and facilitating globalization of CAR-T products and platforms. Prior to that, Dr Dudley served as Director of the Cell Production Facility at the National Cancer Institute where he also led scientific and technical innovation enabling key milestones in immuno-oncology success.

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