Commercial insight: cell and gene therapy

MAY 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.

CELL THERAPY: **Investors looking for an opportunity to gain exposure to gene editing technologies on the public markets were given their second opportunity this past month after Intellia Therapeutics closed its initial public offering raising net proceeds of just under $113 million. One of its close competitors, Editas Medicine, went public only months ago raising $94 million to list on the NASDAQ. Gene editing technologies can be applied as in vivo gene therapies, or be leveraged *ex vivo* to produce cell-based gene therapies. While these cutting edge technologies offer fundamentally game changing advances to the field, investing in their equities comes with the challenge of volatility following go-public transactions. Like many of the cell-based immunotherapy companies that went public in 2015, Editas' massive gains post-IPO were followed by a crash in stock price. For investors that have the risk tolerance appropriate for early-stage platform technologies poised to enter the clinic, Editas and Intellia are buy and hold for the long-term. What is yet to be determined is who will win the ongoing patent battle over CRISPR/Cas9 claims, which will be a future twist that adds further volatility to the system.**

GENE THERAPY
Alan Boyd
CEO, Boyds, UK

CELL THERAPY
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GENE THERAPY: The announcement between Biogen and U. Penn is yet another example of Big Pharma discovering the value of taking cell and gene therapy products seriously. They were there at the dawn of gene therapy development and then got 'cold feet' and avoided the area, particularly after the death of Jesse Gelsinger. However now that most of the hard work has been done by small companies and academic groups and as some of these products have come closer to market, 'Big Pharma' has come back in – well...better late than never!

WORLD'S FIRST PEDIATRIC GENE THERAPY GETS EU APPROVAL

GlaxoSmithKline (GSK) has received European approval for Strimvelis, an *ex-vivo* stem cell gene therapy for the treatment of a Severe Combined Immunodeficiency due to Adenosine Deaminase deficiency (ADA-SCID).

Adenosine deaminase deficiency is a rare, autosomal recessive metabolic disease characterized by severe combined immunodeficiency. Due to the weak immune system with which the babies are born, the disease is sometimes referred to as "bubble baby" disease. It occurs in fewer than one in 100,000 live births worldwide.

Strimvelis was developed by GSK and the Italian institutions, Fondazioine Thelethon and Ospedale San Raffaele. The data supporting the application was collected from 18 children with ADA-SCID. Patients were treated with an autologous $CD34^+$ enriched cell fraction that contained $CD34^+$ cells transduced with a retroviral vector encoding the human ADA cDNA. In order to improve the engraftment of the gene-modified cells, patients were pre-treated with low-dose chemotherapy. All the children (n=18) who contributed to the final data package are alive today (median follow up of 6.9 years). Gene-modified cells were stably present in multiple lineages throughout the follow-up period. The complete trial details and data analysis were recently published in the journal Blood.

The EU approval for Strimvelis had been expected, following a positive opinion from the European Medicines Agency last month. Strimvelis is the third gene therapy to be approved in Europe, after Glybera (for lipoprotein lipase deficiency) and T-Vec (for melanoma).

ISLEXA INTRODUCES NOVEL TECHNOLOGY TO TREAT DIABETES

The Cell and Gene Therapy Catapult (CGT) and University of Aberdeen, UK, have jointly announced the creation of new UK-based company – Islexa – a start-up focused on developing a novel technology

DOI: 10.18609/cgti.2016.026

to produce laboratory grown islets- the organoids responsible for insulin production.

Currently, the UK performs around 50 islet transplants a year, a figure that is a reflection of the lack of donated islets and the risk of complications associated with the procedure. Islexa technology works by reprogramming donated pancreatic tissue into fully functional islets and therefore aims to significantly increase the number of patients who can receive the treatment. The founders hope the technology could dramatically increase the number of patients who can receive transplants of insulin-producing islets.

Professor Kevin Docherty, University of Aberdeen said: "The technology is based on converting pancreatic tissue into functional islets. Islets are organoids that produce multiple hormones, including insulin, and donated islets are already effectively treating severe cases of type 1 diabetes. Having a hugely expanded supply of lab grown islets will enable us to significantly extend this established clinical treatment."

The creation of Islexa follows successful results in pre-clinical studies on the technology and the company will initially continue to focus on further pre-clinical development of the protocol for reprogramming the pancreas tissue into functional islets. Following this, Islexa will be seeking to move towards first-in-human use clinical trials.

Keith Thompson, CEO, Cell and Gene Therapy Catapult and Islexa director commented: "This is a really exciting technology that has the potential to bring life changing benefits to diabetes patients. The collaboration has already delivered promising results and the formation of Islexa will accelerate the development of these lab grown islets and ultimately get this potential treatment to thousands of patients."

GENE THERAPY FOR SANFILIPPO: ABEONA THERAPEUTICS DOSES FIRST PATIENT IN PHASE 1/2 TRIAL

Orchard competitors, Abeona Therapeutics Inc., a US based clinical-stage company, has started its gene therapy (ABO-102) clinical trial in a patient with Sanfilippo Syndrome (Mucopolysaccharidosis Type IIIA or MPSIIIA). This Phase 1/2 trial uses an adeno-associated viral- based gene therapy approach for MPSIIIA and involves a one-time delivery of a normal copy of the defective gene to cells of the central nervous system. The first patient has been enrolled at the Nationwide Children's Hospital (Columbus, Ohio) where the trial will be conducted.

Kevin M. Flanigan, principal investigator with the Center for Gene Therapy at Nationwide Children's Hospital commented: "This investigational gene therapy approach, delivered as a single intravenous injection to treat the whole body, represents a new treatment paradigm for addressing this relentlessly progressing disease".

ABO-102 has been granted Orphan Product Designation in the USA and received the Rare Pediatric

Disease Designation. The clinical study is supported by neurocognitive testing data generated in a 25-subject MPS III Natural History Study, where all patients are through 1 year of follow up assessments.

Timothy J. Miller, Abeona's President and CEO noted: "This first-in-man gene therapy in Sanfilippo patients, helps advance the field of gene therapy with new treatment options for these devastating diseases".

FDA GRANTS ORPHAN DRUG DESIGNATION TO FIBROCELL'S FCX-013 FOR LOCALIZED SCLERODERMA

Fibrocell, an autologous cell and gene therapy company has received orphan drug designation from the US Food and Drug administration (FDA) for their product FCX-013, developed for the treatment of localized scleroderma. 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.

Localized scleroderma encompasses a spectrum of rare diseases causing fibrosis of the skin and underlying tissues, such as fat, fascia and muscle. FCX-013 is an autologous fibroblast cell genetically modified to express a protein to breakdown excess collagen I and III at the site of the localized disease. It incorporates a biological switch (Intrexon Corporation's proprietary RheoSwitch Therapeutic System®), that can be activated by an orally administered compound to allow control of future protein expression once the initial fibrosis has been resolved. FCX-013 is currently in pre-clinical development for the treatment of linear scleroderma, a form of localized scleroderma.

David Pernock, Chairman and Chief Executive Officer of Fibrocell commented: "Achieving orphan drug designation for FCX-013 is an important regulatory milestone for us. We have successfully completed a proof-of-concept study in which FCX-013 reduced the dermal thickness of fibrotic tissue in a scleroderma rodent model. Based on these results, we advanced FCX-013 into pre-clinical dose ranging and toxicology studies for product optimization. We expect to submit an Investigational New Drug application for FCX-013 to the FDA in 2017."

GENE THERAPY TRIAL FOR HEMOPHILIA B SHOWS PROMISE

Spark Therapeutics and Pfizer have announced positive efficacy data from initial subjects in their Hemophilia B Phase 1/2 clinical trial. The trial uses SPK-9001, a bio-engineered adeno-associated virus (AAV) capsid expressing a human Factor IX variant enabling endogenous production of Factor IX. The data will be presented at the 21st

DOI: 10.18609/cgti.2016.026

European Hematology Association's (EHA) Congress on June 11, 2016 by Dr. Spencer Sullivan, one of the trial investigators at the University of Mississippi Medical Center.

Hemophilia B is a rare genetic blood disorder that affects one in 20,000- 30,000 males worldwide. The SPK-9001 trial is led by Dr. Lindsey George of the Children's Hospital of Philadelphia. Subjects in the trial received one-time administration of gene therapy at an initial low dose without the need for immunosuppression. Data obtained from the first three subjects enrolled in the study showed that, AAV-mediated Factor IX levels rose consistently through the first weeks post-administration. Moreover, Factor IX activity sustained at levels exceeding those considered sufficient to reduce the risk of joint bleeds and need for prophylactic clotting factor infusions. SPK-9001 was well-tolerated and no subjects needed immunosuppression.

Spark and Pfizer started their collaboration in 2014. Under the terms of the agreement, Spark will hold responsibility for conducting all Phase 1/2 studies for any product candidates that may be developed under the SPK-FIX program, while Pfizer will ensure responsibility for pivotal studies, any regulatory activities and potential global commercialization of any products that may result from the collaboration.

Katherine A. High, president and chief scientific officer of Spark commented: "We are highly encouraged by these initial data, which are supportive of the target profile of a potential gene therapy product capable of eliminating the need for regular infusions to control and prevent bleeding episodes through a one-time, intravenous administration".

BONE THERAPEUTICS'S ALLOB® PROVIDES POSITIVE EFFICACY DATA FOR BONE FRACTURE REPAIR

ALLOB®, an allogeneic bone cell therapy product developed by Bone Therapeutics for the treatment of delayed-union fractures, showed positive efficacy in a second patient cohort in its Phase I/IIA trial. Seven out of eight patients who received the treatment have met the primary endpoints of the trial within the six-month follow-up period.

The ALLOB® trial is an ongoing, open-label phase I/IIA study designed to evaluate its safety and efficacy in the treatment of delayed-union fractures of long bones, where a single dose of ALLOB® is directly administered at the facture site of the patient percutaneously.

Fracture healing is assessed using radiological and clinical evaluation. In this cohort of eight patients, radiological scores showed an improvement of 77% at six months. Pain at the fracture site improved by 68% and health status by 50% at six months, all data being statistically significant.

Enrico Bastianelli, CEO of Bone Therapeutics commented: "We are pleased to report that these efficacy data for the second cohort are in

line with the positive results communicated for the first and come alongside confirmation of safety in the trial. The clinical and radiological improvements demonstrate that a single administration of ALLOB® can offer significant benefits for these patients and strengthen our belief in the value of this allogeneic 'off the shelf' product."

ADURO BIOTECH'S IMMUNOTHERAPY TRIAL – MAJOR SETBACK FOR PANCREATIC CANCER TREATMENT

Aduro Biotech, Inc., an international immunotherapy company has halted its ECLIPSE trial following disappointing results from Phase IIb clinical trials in metastatic pancreatic cancer patients. The trial evaluated the safety, immune response and efficacy of the combination immunotherapy of CRS-207 with GVAX Pancreas and CRS-207 alone, compared to chemotherapy. The primary endpoint of the trial was overall survival. Although the immunotherapies were generally well tolerated by the patients, the results showed no significant improvement in their overall survival rate.

However, despite the misfortune that has befallen the ECLIPSE trial, the company is hopeful about their ongoing STELLAR trial. This trial evaluates CRS-207 and GVAX Pancreas with and without the anti-PD1 checkpoint inhibitor, nivolumab as a second-line therapy for patients with metastatic pancreatic cancer. "We believe the scientific rationale for combining CRS-207 with a checkpoint inhibitor is compelling" said Stephen T. Isaacs, Chairman, President and CEO of Aduro.

ADURO BIOTECH PANCREATIC FAILURE

GVAX, a therapeutic composed of irradiated tumour cells modified to express GM-CSF, may be nearing its end after Aduro posted disappointing results in a phase 2 study of GVAX in combination with its engineered Listeria product CRS-207. GVAX has been in clinical development for years and generally failed to demonstrate efficacy as a single agent, which allowed Aduro to purchase the asset at a bargain price from BioSante back in 2013. Aduro was hoping that combining the technology with CRS-207 would unleash its efficacy but, in an unexpected turn, the combination delivered less than either CRS-207 or chemotherapy alone in the solo arms. - ***Mark Curtis***

DOI: 10.18609/cgti.2016.026

CELLECTIS' 'DESIGNER' CELLS CURE CANCER IN A SECOND CHILD

It's been reported that a second child with acute lymphoblastic leukaemia (ALL) who received the experimental UCART19 injection is free of cancer six months after treatment. The case was presented at the American Society of Gene & Cell Therapy annual meeting in Washington. The first case, a two-year-old child, continues to be in remission 11 months after treatment. Andre Choulika, CEO of Collectis commented: "This is not a statistical proof but we do now have two cases. It shows that the therapy has some potential." Both the children received treatment on compassionate grounds at the Great Ormond Street Hospital, London. Clinical trials of UCART19 are scheduled to begin in 2016.

Cellectis' UCART19 is developed from third party healthy donors, unlike other CAR-T therapies which use modified cells extracted from patients' own blood. ''Allogeneic therapies are going to be more affordable and more available than personalized treatments", said Choulika. Shares in Cellectis gained as much as 14% after the company announced this news on May 6th, 2016.

CALADRIUS' TREATMENT FOR TYPE 1 DIABETES GETS ORPHAN DRUG STATUS

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

In additional news this month, Caladrius Biosciences, also announced the licensing of exclusive global rights to its cell technology for the treatment of ovarian cancer, to AiVita Biomedical, Inc. Under the terms of the agreement, AiVita will hold responsible for all costs to develop a product using the licensed intellectual property. In return, Caladrius will receive certain development milestone payments as well as royalties on sales of any commercial product. This transaction supports the Caladrius's strategy to monetize non-core assets.

The license contributes to AiVita's intellectual property protection for its next generation immunotherapy targeting cancer stem cells. AiVita intends to begin a Phase II clinical trial to evaluate the efficacy of its novel appoach for ovarian cancer in 2016. To facilitate these clinical objectives, AiVita has also assumed a sublease of the Caladrius's former Irvine, California facility. This sublease obligation will cover for the remainder of the lease term all cash obligations of Caladrius with respect to the rent and overhead of the Irvine facility.

STEMCELLS, INC. TERMINATES PHASE II PATHWAY TRIAL IN SPINAL CORD INJURY

StemCells, Inc., a clinical research company specialized in using cell-based therapeutics in CNS disorders, have announced its decision to terminate the phase II Pathway Study in spinal cord injury following a review of data. Although the results showed improvement in patients treated with StemCells' proprietary HuCNS-SC human neural stem cells, the magnitude and trend of the effect over time did not justify continuation.

The Pathway Study was a single-blind, randomized, controlled clinical trial investigating the use of HuCNS-SC human neural stem cells for the treatment of chronic spinal cord injuries. Interim analysis of Cohort II data concluded that achieving the primary endpoint objective of the pathway study was unlikely. Based on this finding, the company has decided to terminate the study and close out operations. It will present the Cohort 1 and interim analysis data at the 14th Annual Meeting of the International Society for Stem Cell Research (ISSCR) in San Francisco, California, on June 23, 2016.

Dr. Stephen Huhn, Chief Medical Officer and VP of StemCells' Clinical Research commented: "The collective human data we have generated across all of our studies reinforce our belief that our cells have an excellent safety profile and that there are neurological and retinal disorders with unmet need that may be helped by cell transplant. Unfortunately, the company does not have the resources to implement changes in our development program to permit further investigation."

Following trial termination decision, the board of directors have also approved a plan to wind down the Company. As part of this process, the company will evaluate opportunities to monetize its intellectual property.

STEMCELLS INC. TO SHUT DOWN

After decades researching stem cell therapies, industry pioneer StemCells Inc. announced it will be winding down its operations following a failed phase 2 study investigating its fetal neural stem cell product in patients with spinal cord injury. It's disappointing news, especially given that the number of true cell-based regenerative medicine companies has dwindled over the years. However, Neuralstem and Asterias Biotherapeutics will continue to hold the torch and develop cell therapies for spinal cord injury. Like StemCells Inc., Neuralstem is developing neural progenitor cells derived from fetal spinal cord tissue. Asterias is taking a different route, using pluripotent stem cell-derived oligodendrocyte progenitors. - ***Mark Curtis***

DOI: 10.18609/cgti.2016.026

KITE PHARMA'S KTE-C19 RECEIVES ORPHAN DRUG DESIGNATION FROM FDA

The US FDA has granted orphan drug designation to Kite Pharma's KTE-C19 for the treatment of primary mediastinal B cell lymphoma (PMBCL), mantle cell lymphoma (MCL), follicular lymphoma (FL), acute lymphoblastic leukemia (ALL) and chronic lymphocytic leukemia (CLL). Kite had previously received orphan drug designation for KTE-C19 for the treatment of diffuse large B cell lymphoma (DLBCL) in both the U.S. and the EU, as well as orphan drug designations in the EU for PMBCL, MCL, FL, ALL, and CLL. KTE-C19 is an investigational therapy in which patient's T cells are genetically modified to express a CAR that is designed to target the antigen CD19, a protein expressed on the cell surface of B cell lymphomas and leukemias.

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. Kite is currently enrolling patients with various B cell malignancies for four pivotal studies (also known as ZUMA studies) using KTE-C19.

BLUEBIRD BIO PRESENTED PRE-CLINICAL DATA ON MULTIPLE GENE THERAPY PROGRAMS

Bluebird bio, a clinical-stage company specialized in developing T-cell based immunotherapies presented pre-clinical data from its oncology and hematopoietic stem cell (HSC) gene therapy programs at the *19th Annual meeting of American Society of Gene and Cell Therapy*.

Oncology gene therapy

- Dr Wai-Hang Leung presented data on Daric, a small-molecule regulated antigen recognition system for inducible T-cell targeting of cancer cells. Data also highlighted its scope in treating autoimmune diseases.
- Dr Kevin Friedman demonstrated evidence on a potent CAR targeting B-cell maturation antigen to treat myeloma and some lymphomas. It also showed how modulating PI3K pathway during manufacturing process can increase the potency and fitness of CAR T cells.
- Dr Baeckseung Lee presented results on the generation of CAR T cells by homology directed transgene integration into the TCR- alpha locus. This was achieved using megaTALs, a gene editing technology developed by bluebird bio.

HSC gene therapy

- Dr Melissa Bonner presented data on the evaluation of compounds with the potential to increase cell transduction efficiency in lentiviral vectors. Staurosporine showed increased transduction efficacy in human $CD34^+$ cells.
- Dr Garrett C. Heffner showed results on the efficacy of PGE2 in improving vector copy number and enhancing lentiviral transduction in $CD34^+$ cells.

▸ Sarah Slauson's poster depicted a scalable manufacturing process of an inducible producer 293F cell line grown in suspension culture.

Additionally, bluebird's academic collaborators delivered two oral presentations on the ongoing gene therapy trials. Dr David Williams (Dana-Farber/ Boston Children's Hospital) and Dr Marina Cavazzana (University of Paris Descartes) presented interim data from the Starbeam study of Lenti-DTM in cerebral adrenoleukodystrophy and LentiGlobin® in severe sickle cell disease, respectively.

BIOSTAGE SEE FDA APPROVAL FOR CLINICAL TRIALS OF ESOPHAGAL IMPLANT

Biostage, a biotechnology company developing bioengineered organ implants have announced that it has successfully regenerated esophagus in a pre-clinical work conducted in collaboration with Mayo Clinic. The company currently expects to file an IND application with the US FDA in late 2016. The IND seeks approval to initiate clinical trials for its esophageal implants in humans.

Biostage uses a technology which combines a proprietary biocompatible scaffold with patient's own stem cells to create organ implants. The pre-clinical study was performed in animal models where esophageal implants, consisting of a proprietary biocompatible synthetic scaffold seeded with the recipient animal's own stem cells, were surgically implanted in place of the esophagus section that had been removed. Results demonstrated the successful regeneration of esophagal sections from the organ implants. The animals in the study showed no significant side effects. Dr. Dennis Wigle, Associate Professor of Surgery and Chair of Thoracic Surgery at Mayo Clinic, and Dr. Saverio La Francesca, Chief Medical Officer of Biostage, are principal investigators for the study.

Dr Saverio La Francesca commented: "Beyond the unparalleled evidence of tissue regeneration, we are also very encouraged that there has been no evidence of leakage or infection at the surgery sites in any of the animals studied so far. Such issues pose regular and life-threatening dangers for esophageal cancer patients surgically treated with the existing standards of care. These results represent a dramatic step forward in our quest to bring new solutions to patients with life-threatening conditions."

BIOSTAGE REGENERATES ESOPHAGUS IN PC STUDIES

Biostage, formerly Harvard Apparatus Regenerative Technology, is pushing the envelope in tissue engineering. The company has now shown that its Cellspan platform, composed of a biocompatible synthetic scaffold seeded with autologous stem cells, is capable of regenerating functioning esophageal segments in a large animal model. Biostage will deploy the platform to replace tissue for oncology applications involving the esophagus, trachea and bronchus. An IND will be filed for Biostage's Cellspan Esophageal implant in 2016. - *Mark Curtis*

DOI: 10.18609/cgti.2016.026

BIOGEN TO TEAM UP WITH UPENN ON MULTIPLE GENE THERAPY PROGRAMS

In a move towards advancing gene therapy and gene editing technologies, Biogen have entered into collaboration with University of Pennsylvania (UPenn) on multiple gene therapy programs. UPenn is expected to receive up to $2 billion in research funding, options and milestone payments from Biogen.

The team will primarily focus on the development of therapeutic approaches that target the eye, skeletal muscle and central nervous system. The alliance will also work on validating gene transfer technologies using AAV delivery vectors and genome editing technologies.

Olivier Danos, senior vice president, Cell & Gene Therapy at Biogen commented: ''By exploring next-generation delivery in various tissues such as the retina, skeletal muscle and CNS, we will explore the potential for extending gene therapy beyond disorders linked to single gene mutations and into a broader spectrum of complex diseases, including devastating neurological conditions that affect a multitude of patients throughout the world."

SEATTLE CHILDREN'S & JUNO THERAPEUTICS COLLABORATE IN THE FIGHT AGAINST BRAIN CANCER

Seattle Children's have entered into collaboration with Juno Therapeutics to accelerate their T-cell immunotherapy clinical trials for children and adults with brain tumors (gliomas). The goal of the collaboration is to open Phase 1 clinical trials within the next two years.

The collaboration will ensure Juno's support through sponsorship of research and a license agreement with respect to CAR T-cell technology developed at Seattle Children's Research Institute. The pediatric clinical trial will be conducted at Seattle Children's Hospital. The trial is funded in part by Strong Against Cancer, a national philanthropic initiative with worldwide implications for curing childhood cancers through immunotherapy treatments.

Dr. Mike Jensen, Director of Ben Towne Center for Childhood Cancer Research at Seattle Children's Research Institute commented: "Brain cancer is a devastating disease. Current treatments for brain tumors like radiation can do irreparable harm, especially on a child's developing brain, and greatly diminish the quality of life for survivors. We believe the immune system holds the promise of offering safe and effective treatment of brain cancers, while preserving brain function.

ORCHARD THERAPEUTICS & UMI3 COLLABORATE ON HUMAN TRIALS USING STEM CELL GENE THERAPY

Scientists at the University of Manchester, UK, have developed a stem cell gene therapy approach to reverse a fatal childhood illness: Sanfilippo disease and are due to work in partnership with Orchard Therapeutics to move forward to clinical trials.

University of Manchester and Central Manchester University Hospital NHS Foundation Trust (CMFT) researchers have developed the pioneering approach to treat Sanfilippo disease (also known as mucopolysaccharidosis type III or MPS III). Sanfilippo is caused by a lack of the SGSH enzyme, which helps to break down and recycle long chain sugars. Lack of SGSH results in a build-up of sugars in the body and particularly the brain.

Dr Brian Bigger, who leads the Stem Cell and Neurotherapies Laboratory at The University of Manchester and developed the technique in partnership with the Trust scientists said: ''This licence agreement with Orchard will allow us to take the technique we have developed to the next and crucial stage of trials in humans. We are hopeful that this treatment may help to treat the early onset dementia in these patients and saving children's lives.

Following a licence agreement with Orchard Therapeutics, a new UK-based clinical-stage biotechnology company, the gene therapy developed in Manchester will be trialled in humans. The University of Manchester's technology transfer company, UMI3, negotiated the terms of the deal with Orchard Therapeutics, which have not been disclosed.

Professor Robert Wynn, Consultant Paediatric Haematologist at Royal Manchester Children's Hospital and chief investigator for the clinical study explained: 'This new clinical study aims to explore whether we can use stem cell gene therapy to produce blood cells that express corrected versions of the missing enzyme.

The recent approval of Strimvelis from GSK has demonstrated that combined stem cell gene therapy based products are capable of being given marketing approval by the regulators. This was also the first product to be approved that uses a lentivirus as a vector - therefore it's positive to see that similar type of products are progressing towards the clinic. Orchard Therapeutics has recently been established to develop such products and to build on this, and it has now been announced that they are acquiring, under licence, the programme to develop a treatment for Sanfilippo Disease from Manchester University. Through this partnership it will allow the product to progress into clinical trials and provide evidence that single-gene brain diseases can be treated by the stem cell gene therapy approach. The product also uses a lentivirus as the vector which has been engineered to make it more specific to white cells that traffic into the brain after its establishment in the bone marrow following transplantation. If this approach works, then it will open up the route to treat other such monogenic bone marrow disorders. All good news - ***Alan Boyd.***

DOI: 10.18609/cgti.2016.026

IMMUNOCELLULAR THERAPEUTICS TO RECEIVE LOGISTICS SUPPORT FROM BIOLIFE SOLUTIONS & MNX GLOBAL LOGISTICS

BioLife Solutions, Inc. have partnered with MNX Global Logistics to support ImmunoCellular Therapeutics' phase III clinical trial. The trial uses ICT-107 dendritic cell- based immunotherapy to treat patients with newly diagnosed gliablastoma. MNX will use their logistics service to ship the apheresis starting material, from which ICT- 107 is manufactured to produce personalized treatment for each patient involved in the trial.

Marta Schilling, Vice President, Cell Therapy Manufacturing at ImmunoCellular Therapeutics, stated: "Through MNX's partnership with BioLife, we were introduced to the evo Smart Shipper and biologistex cold chain SaaS. This is a state-of-the-art approach that we will use to enhance MNX's logistics services to ensure that our time and temperature-sensitive apheresis starting material arrives intact and according to specifications at our clinical manufacturing partner sites.

EDITAS MEDICINE PARTNERS WITH CYSTIC FIBROSIS FOUNDATION THERAPEUTICS

Editas Medicine, a genome editing company, has entered into a three-year agreement with Cystic Fibrosis Foundation Therapeutics, Inc. (CFFT), the non-profit affiliate of the Cystic Fibrosis Foundation. The agreement aims to support the development of CRISPR/Cas9-based medicines for the treatment of cystic fibrosis (CF). Under the terms of the agreement, CFFT will pay up to 5million dollars to Editas and provide access to its extensive network of CF scientific experts and clinical researchers.

CF is caused by mutations in a gene that codes for cystic fibrosis transmembrane conductance regulator protein. More than 1,800 CFTR mutations have been identified so far. As part of this agreement, Editas Medicine will investigate to target both common mutations as well as mutations not addressed by conventional approaches.

Preston W. Campbell III, President and Chief Executive Officer of CF Foundation commented: "We believe that the CRISPR approach to gene editing holds significant promise for repairing the underlying cause of cystic fibrosis and we are pleased to work with Editas Medicine and are excited by the possibilities of what can be accomplished on behalf of people with CF."

CARIBOU BIOSCIENCES RAISES $30 MILLION IN SERIES B FUNDING

Caribou Biosciences, Inc., a US based company specialized in genome engineering, have announced the completion of a $30 million Series B financing round. It also announced a new addition to company's board of directors - Philip Austin, Founding Partner at Anterra Capital. Heritage Group, Anterra Capital, Maverick Capital Ventures, and Pontifax AgTech were the new investors who participated in the financing. The existing investors, F-Prime Capital Partners, Novartis, Mission Bay Capital, and 5 Prime Ventures also participated in the round.

"The proceeds from this financing will enable us to continue to expand our industry-leading CRISPR gene editing technology platform and accelerate our efforts in highly promising application areas in agriculture, therapeutics, biological research, and industrial biotechnology. We look forward to working with this outstanding group of investors, and bringing their deep expertise and guidance to bear as we deliver on the promise of our technology platform." Rachel Haurwitz, Ph.D., President and Chief Executive Officer and co-founder of Caribou.

CRISPR-Cas technologies for genome engineering have received a large amount of interest recently and the focus continues with the announcements from Agenovir, Caribou Biosciences and Editas Medicine. All three companies announced deals or collaborations relating to funding and/or support from larger organisations and in these cases the Cystic Fibrosis Foundation and Celgene. Clearly the basic premise that this technology will work appears to have been accepted and now companies such as these have raised the funds with particular but very different therapeutic approaches that are being developed. In the case of Agenovir the technology is being applied to treat persistent viral infections, whilst at Editas, it is being applied to the discovery and development of treatments for Cystic Fibrosis. Perhaps the time has come not only to have meetings relating to Cell and Gene Based Therapies but to Cell, Gene and Gene Editing Based Therapies and will ASCGT and ESCGT have to change their names again? *Alan Boyd*

DOI: 10.18609/cgti.2016.026

INTELLIA THERAPEUTICS ANNOUNCES CLOSING OF IPO

Intellia Therapeutics, Inc., a pharmaceutical company specializing in gene editing technology using CRISPR/Cas9 have announced the closing of its initial public offering of 6,900,000 shares of common stock at a public offering price of $18.00 per share. This includes the exercise in full by the underwriters of their option to purchase up to 900,000 additional shares of common stock. Shares began trading on the NASDAQ Global Select Market on May 6, 2016. The net proceeds of the offering to Intellia were approximately $112.9 million, after deducting underwriting discounts and commissions and estimated offering expenses. Credit Suisse, Jefferies LLC and Leerink Partners acted as joint book-running managers for the offering. Wedbush PacGrow acted as lead manager.

AGENOVIR RAISES $10.6 MILLION IN SERIES A FINANCING

Agenovir Corporation, a California- based antiviral therapeutic firm, have announced that it raised $10.6 million in a Series A financing. The round was led by Data Collective with participation from Celgene Corporation, Lightspeed Venture Partners and several prominent individual and other investors.

Agenovir was founded based on technology developed in the laboratory of Prof. Stephen Quake, Stanford University and Howard Hughes Medical Institute. The company is using CRISPR/Cas9 and other computationally designed nuclease technology to disrupt intracellular viral DNA.

The company will use the funds to increase the infrastructure, continue to build up the intellectual property portfolio, and advance key therapeutic candidates into clinical development.

KITE PHARMA APPOINTS PAUL L. JENKINSON AS CHIEF FINANCIAL OFFICER

Kite Pharma, Inc. have announced the appointment of Paul L. Jenkinson as Chief Financial Officer. Mr. Jenkinson succeeds Cynthia M. Butitta, who will continue as Kite's Chief Operating Officer.

Mr. Jenkinson was formerly Vice President of Global Commercial and Corporate Finance at Allergan. He was responsible for the corporation's financial planning and analysis activities, working with commercial operations, manufacturing operations, research and development, and general and administration functions in multiple international markets. He began his career in finance positions at Deloitte New Zealand and

later at a predecessor company of Fonterra. Following that, he was Vice President at Black & Decker Corporation and corporate officer at Kwikset, Baldwin and Weiser Lock Companies.

FATE THERAPEUTICS APPOINTS NEW CHIEF MEDICAL OFFICER

Fate Therapeutics, Inc. a biopharmaceutical company specialized in the development of cellular immunotherapies for cancer and immune disorders has announced the appointment of Dr Chris M. Storgard as its chief medical officer.

Dr Storgard has more than 20 years of experience in clinical drug development and joins Fate Therapeutics from Ardea Biosciences, a member of the AstraZeneca Group, where he was Vice President of Clinical Research and Development. At Ardea, Dr. Storgard led the ZURAMPIC® global clinical program to successful US and European regulatory approvals. Before joining Ardea, Dr Storgard held senior positions in drug development and medical affairs at Prometheus Laboratories, Biogen Idec and Amgen.

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DOI: 10.18609/cgti.2016.026