Commercial insight: cell and gene therapy

SEP 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
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GENE THERAPY: This month sees exciting developments in the clinical arena, with Bluebird Bio announcing the initiation of a Phase 3 clinical trial in transfusion-dependent beta-thalassemia, and Alnylam announcing positive initial data from its Phase 1 study in healthy volunteers, investigating its RNAi therapeutic targeting glycolate oxidase for the treatment of Primary Hyperoxaluria Type 1. Alnylam has a rich pipeline of RNAi therapies and, with its announcement of plans for a European hub in the UK, is clearly confident in its future value and success. Balancing this positive news is the announcement of the disbandment of Novartis's cell and gene therapy unit. Although the company has committed to continuing to develop CAR-T therapies, this can only be seen as a blow to the field, and is reflected in the negative effects on the valuations of fellow CAR-T players Kite and Juno.

CELL THERAPY: Industry and investors alike have placed their bets on autologous T-cell immunotherapies as the future of oncology. Some have deviated from the pack and made advances on the allogeneic side, namely Cellectis, which is developing gene-edited donor-derived T cells that evade immune detection. Although progress with directed differentiation of

pluripotent cells to T cells is a threat that could disrupt the current trajectory. Fate Therapeutics announced a deal with Memorial Sloan Kettering Cancer Center (MSKCC) this past month that will focus on the development of a truly scalable platform for the production of engineered T cells from pluripotent sources. While directed differentiation has a complex IP space, Fate will lay exclusive claim to patents recently generated at Sloan Kettering for the production of both T and NK cells.

ASTERIAS'S STEM CELL TRIAL SHOWS POSITIVE EFFICACY DATA

Asterias Biotherapeutics, a US-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 complete cervical spinal cord injury patients.

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

Data presented by Dr Edward Wirth, CMO of Asterias, at the 55th Annual Scientific Meeting of the International Spinal Cord Society in Vienna showed that all five patients in the second cohort have shown at least one motor level of improvement so far and two patients in the cohort have achieved two motor levels of improvement on at least one side of their body. Patient improvements are being measured by the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) neurological classification scale widely used to quantify functional status of patients with 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. Last month 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: "The results to date in the 10 million cell cohort, while still early, demonstrate meaningful improvement in motor function, particularly in the use of a patient's hands, fingers and arms, which is critically important for a patient's quality of life and ability to function independently. We are quite encouraged by this first look at efficacy results and look forward to reporting 6-month efficacy data as planned in January 2017. We have also just recently been cleared to begin enrolling a new cohort and administering to these new patients a much higher dose of 20 million cells. We look forward to begin evaluating efficacy results in this higher-dose cohort in the coming months as well."

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EXPERT PICK

PROGRESS IN SPINAL CORD INJURY

Asterias Biotherapeutics posted positive efficacy data in its clinical study investigating human embryonic stem cell-derived oligodendrocyte progenitors in patients with complete spinal cord injury. Patients treated with 10M cells showed motor improvements in the upper body on both sides, and it would appear there could be a dose-related response emerging. This is uplifting news, following the recent departure of StemCells, Inc. The next cohort of patients will be dosed with 20M cells. Asterias is another example of a company making headway with a pluripotent platform. – *Mark Curtis*

BLUEBIRD BIO INITIATES PHASE 3 TRIAL FOR BETA-THALASSEMIA

bluebird bio, a clinical-stage company specialized in developing lentiviral-based gene therapies for severe genetic diseases, has announced the initiation of its Phase 3 gene therapy trial in patients with transfusion-dependent beta-thalassemia.

The study, HGB-207, is a Phase 3, global, multi-center study designed to evaluate the safety and efficacy of gene therapy in subjects with transfusion-dependent beta-thalassemia by transplantation of autologous CD34+ cells transduced *ex vivo* with a lentiviral β-A(T87Q)-globin vector (LentiGlobin™ BB305).

The trial will include the addition of two transduction enhancers to the hematopoietic stem cell (HSC) manufacturing process to increase transduction efficiency. The rationale for this modified protocol arises from accumulating clinical data that shows a correlation between vector copy number, percentage of vector-containing cells and the amount of hemoglobin produced by patients treated with LentiGlobin. The study will be conducted under the same investigational new drug (IND) application as other studies of LentiGlobin in beta-thalassemia.

The primary end point of the study is transfusion independence, defined as a 12-month transfusion-free period after HSC transplantation. This study is intended to be pivotal in the USA and confirmatory in the EU.

LentiGlobin™ BB305 is currently in three clinical studies for the treatment of transfusion-dependent beta-thalassemia and severe sickle cell disease.

Dr David Davidson, bluebird's chief medical officer, commented: "We believe that the addition of our transduction enhancers to our manufacturing process has the potential to substantially increase the hemoglobin levels in patients with transfusion-dependent beta-thalassemia and increase their likelihood of achieving clinically meaningful reductions in transfusion requirements or transfusion independence, the ultimate goal of our therapy."

NOVARTIS DISSOLVES ITS CELL & GENE THERAPIES UNIT

Novartis, a Switzerland-based biopharmaceutical company, has announced the dissolution of its Cell and Gene Therapies Unit as part of its internal re-organizational design. The company aims to re-integrate the activities of the unit into the larger Novartis organization.

Working with University of Pennsylvania (UPenn), the Cell and Gene Therapies Unit at Novartis has advanced one of the leading chimeric antigen receptor T-cell (CAR-T) therapies now in pipeline, as it battles against Kite and Juno to be the pioneers to bring CAR-T therapies to the market.

Although it appears to be a death blow to the CAR-T field, Novartis has confirmed that it is committed to the continued development of CAR-T therapies and the company's decision is to re-integrate activities conducted by the unit into the larger Novartis organization.

Novartis has seen great success in the CAR-T field, especially with its investigational CAR-T therapy, CTL019, for the treatment of children with relapsed/refractory acute lymphoblastic leukemia. Mid-stage trial results reported in late 2015 showed that the treatment wiped out the blood cancer in 93% of patients. The company plans to submit regulatory approval applications to the US FDA and EMA in 2017.

Novartis has confirmed that its 400-member group is being disbanded, with most being redeployed to new positions while 120 could be left without a job.

The news has hit hard on Kite and Juno, with shares dropping 4 and 5%, respectively.

Novartis and UPenn have an exclusive global collaboration to develop and commercialize CAR-T cell therapies for the treatment of cancer. The company has confirmed that this organizational change will not impact the terms and conditions of the agreement and that it looks forward to advancing CAR-T therapies.

FDA GRANTS ORPHAN DRUG DESIGNATION FOR FATE THERAPEUTICS' PROTMUNE™

Fate Therapeutics, a biopharmaceutical company specialized in the development of cellular immunotherapies for cancer and immune disorders, has received orphan drug designation from the US Food and Drug Administration (FDA) for its lead product candidate, ProTmune™. The designation is granted for the "prevention of graft-versus-host disease in patients undergoing allogeneic hematopoietic cell transplantation (HCT)" and covers diseases including blood cancers and genetic disorders.

The trial is designed as an open-label, Phase 1/2, multi-center clinical study for the prevention of acute GvHD and cytomegalovirus (CMV) infection, both of which are leading

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causes of morbidity and mortality in patients undergoing HCT. ProTmune™'s cell therapy is produced by modulating a donor-sourced, mobilized peripheral blood graft *ex vivo* with two small molecules (FT1050 and FT4145) to enhance the biological properties and therapeutic function of the graft's immune cells. The programmed mobilized peripheral blood graft is adoptively transferred and administered to a patient as a one-time intravenous infusion.

Scott Wolchko, CEO of Fate Therapeutics, commented: "The granting of both orphan drug and Fast Track designations for ProTmune validates the product candidate's unique therapeutic potential to address life-threatening complications and improves the curative potential of allogeneic HCT. Through our development of ProTmune, we seek to transform the allogeneic HCT paradigm by providing immunocompromised patients a therapeutically optimized donor graft containing immune cells with reduced alloreactivity and enhanced infection-fighting and anti-tumor properties."

ALNYLAM'S RNAI THERAPEUTIC PROVIDES HOPE FOR PRIMARY HYPEROXALURIA PATIENTS

Alnylam, a Cambridge, MA-based biopharmaceutical company specialized in the development of RNAi-based therapeutics, has announced the initial results of its ongoing Phase 1/2 study for the treatment of primary hyperoxaluria type 1 (PH1).

PH1 is an inborn error of metabolism and is a rare genetic disease characterized by excessive oxalate accumulation in plasma and urine, resulting in calcium oxalate crystal formation and deposition in the kidney and many other tissues. It arises from mutations in the enzyme alanine-glyoxylate aminotransferase.

This Phase 1/2 trial of ALN-GO1 is a randomized, single-blind, placebo-controlled study aimed to evaluate the safety and tolerability of single and multiple subcutaneous doses of ALN-GO1. ALN-GO1 is an investigational RNAi therapeutic targeting glycolate oxidase (GO). The study is conducted in two parts: part A is a single-dose study conducted in 32 healthy adult volunteers and part B will be a multi-dose study designed to enroll up to a total of 20 patients with PH1. The secondary objectives of the study include evaluation of pharmacokinetics and clinical activity for ALN-GO1 as measured by its effects on plasma glycolate and urinary oxalate levels in normal healthy volunteers and PH1 patients, respectively.

The initial part A clinical results were presented at the 17th Congress of the International Pediatric Nephrology Association (IPNA) in Brazil. Results indicated that single, subcutaneous doses of ALN-GO1 showed dose-dependent increases in plasma and urine glycolate. Increases in plasma and urine glycolate in healthy volunteers confirm effective GO knockdown and provide preliminary human proof of concept for ALN-GO1. In addition, ALN-GO1 was safe and well tolerated by the subjects without any serious adverse events. The company plans to initiate part B of the Phase 1/2 study.

Akshay Vaishnaw, CMO of Alnylam, commented: "We believe these initial results are encouraging, as they demonstrate preliminary human proof of concept for this novel investigational RNAi therapeutic. We now look forward to advancing this program into patients in part B of the ongoing Phase 1/2 study, where we aim to achieve lowering of urinary oxalate, which is known to deposit in kidneys and cause extensive renal and broader tissue damage in patients with PH1."

Alnylam's announcement of positive data from the first part of a Phase 1/2 study in healthy adult volunteers will provide encouragement to patients with primary hyperoxaluria type 1 (PH-1). The company has a diverse pipeline of projects based around RNAi technology, but as yet no approved products. ALN-GO1 targets glycolate oxidase (GO), and data from the Phase 1/2 study show evidence of effective knock-down of the enzyme, which has the potential to reduce excessive oxalate in PH-1. There remain significant hurdles ahead, not least the question of whether evidence of enzyme knock-down and any associated metabolic effects are sufficient for approval, or whether clinical benefits such as inhibition of kidney stone formation will be required in the clinical package. – *Richard Philipson*

KITE'S CAR-T THERAPY SHOWS POSITIVE RESULTS IN NON-HODGKIN LYMPHOMA PATIENTS

Kite Pharma, a California-based biopharmaceutical company specialized in the development of cancer immunotherapy products, has announced positive interim data of its ZUMA-1 trial in patients with chemorefractory diffuse large B-cell lymphoma (DLBCL).

The ZUMO-1 trial uses Kite's lead product candidate, KTE-C19, an investigational therapy in which a patient's T cells are genetically modified to express a chimeric antigen receptor (CAR) designed to target the antigen CD19, a protein expressed on the cell surface of B-cell lymphomas and leukemias.

ZUMA-1 enrolled chemorefractory non-Hodgkin lymphoma (NHL) patients into two cohorts: cohort 1 enrolled patients with DLBCL and cohort 2 included patients with transformed follicular lymphoma (TFL) and primary mediastinal B-cell lymphoma (PMBCL). The interim analysis of ZUMA-1 evaluated the objective response rate (ORR) in the first 51 patients in cohort 1 with at least 3 months of follow-up and an additional 11 patients in cohort 2. KTE-C19 met the primary end point with ORR of 76%, including 47% complete remissions.

The most common adverse events observed in the patients included neutropenia, anemia, febrile neutropenia, thrombocytopenia and encephalopathy. The study also

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saw the death of two patients due to KTE-C19-related adverse events.

KTE-C19 was granted Breakthrough Therapy Designation by the US FDA in 2015 for the treatment of DLBCL, PMBCL and TFL. It also gained access to the European Medicines Agency (EMA)'s Priority Medicines support, for the treatment of DLBCL earlier this year. Kite aims to apply for regulatory approval of KTE-C19 in DLBCL, TFL and PMBCL based upon the combined data of both cohorts.

Arie Belldegrun, Chief Executive Officer of Kite Pharma, commented: "What started at the NCI over a decade ago with the pioneering work of Steven A Rosenberg has evolved into a technology that has the potential to fundamentally change the outlook of patients with cancer. I'm proud of what we've achieved to date and excited to apply our advanced learnings from ZUMA-1 to our ongoing clinical development programs to bring continued innovation to patients and the scientific community at large."

I ZUMA-1 STUDY

Interim data from Kite's ZUMA-1 study in patients with a variety of aggressive lymphomas showed an objective response rate of 76% and overall response rate of 47%, meeting its primary end points. Follow-up has reached 3 months across the 62 patients in the study. What will be critical to commercialization of the product is the 6- and 9-month data to come in 2017, which will need to show durability of patient response to appease regulators and payers. Kite is well positioned as a leader in CAR-T for liquid cancers, as recent complications have set Juno back and Novartis has weakened its stance. Kite also announced a deal with the NIH to gain exclusive access to a number of TCR products targeting mutated KRAS antigens for a variety of solid tumors, which puts even more wind in its sails. – *Mark Curtis*

KERASTEM INITIATES CELL THERAPY TRIAL FOR BALDNESS

Kerastem Technologies, a US-based company specialized in advanced hair therapy, has initiated a Phase 2 clinical trial using cell-enriched adipose for the treatment of androgenetic alopecia.

The trial named as STYLE is a prospective, randomized, multi-center device trial aimed to evaluate the safety and efficacy of the Celution and Puregraft Systems in the processing and preparation of an autologous fat graft enriched with adipose-derived regenerative cells (ADRCs) in the treatment of early alopecia androgenetica.

The procedure includes a fat harvest using micro-liposuction followed by the processing and purification of lipoaspirate in the Puregraft and Celution System, respectively. Subjects will be randomly assigned to receive a subcutaneous scalp injection of either a fat graft cell

enriched with ADRCs (available in two different doses), a fat graft without cell enrichment using a blood saline solution (fat alone control) or a saline injection (no-fat control) in a 2:2:2:1 ratio. The primary end point of STYLE is safety and tolerability at 6 months and subjects will be followed for 12 months. The trial, which will be conducted in up to 8 centers in the USA, is expected to complete by March 2017.

Kerastem also holds global rights to commercialize Cytori Therapeutics' autologous cell therapies for alopecia and hair related indications.

GSK AMENDS AGREEMENT WITH MOLMED TO EXPAND ITS GENE THERAPY PORTFOLIO

MolMed, a Milan-based medical biotechnology company has announced the amendment of its strategic agreement with GlaxoSmithKline (GSK) concerning MolMed's supply of development, manufacturing and technology transfer services for the clinical application of viral vector-based gene therapies.

MolMed entered into a 5-year strategic collaboration with GSK on the 19th of March 2015. Prior to this, the company had collaboration with GSK for the development of Strimvelis, an *ex vivo* stem cell gene therapy for severe combined immunodeficiency caused due to adenosine deaminase deficiency (ADA-SCID). These long-lasting and successful collaborations have resulted in an increased demand of MolMed's resources necessary for GMP manufacturing of cell and gene therapy for the GSK programs. Based on this, the companies have amended its strategic agreement on the 1st of September 2016.

Under the terms of the agreement, Molmed will be eligible for a minimum anticipated revenue of €48 million instead of the €34 million that was agreed 18 months ago. In return, GSK will have the access to Molmed's expanded expertise and capabilities in gene therapy.

Riccardo Palmisano, CEO of MolMed, commented: "We are very pleased with the new terms of the agreement with GSK. The additional minimum revenues anticipated through the 5 years-period covered by the contract, will clearly benefit one of the two pillars on which our company plans to build its growth: the supply of sophisticated services in cell and gene therapy field, where MolMed strongly invested, developing state-of-the-art laboratories and increasing its production capacity."

PCT SIGNS MANUFACTURING SERVICES AGREEMENT WITH ADAPTIMMUNE

PCT, a manufacturing service provider subsidiary of Caladrius Biosciences has announced a new 5-year strategic manufacturing services agreement with Adaptimmune Therapeutics for

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the production of Adaptimmune's 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. PCT, through its specialized staff and facilities, will manufacture the SPEAR T-cell products from development through to clinical manufacturing and commercialization. The company will produce the products at its New Jersey facility in a manner compliant with both US FDA and EMA regulations.

Dr Gwendolyn Binder-Scholl, Adaptimmune's CTO, commented: "PCT is an elite contract manufacturing organization in the field of patient-specific cell therapies, and we are very pleased to strengthen and develop our existing relationship. We have worked with PCT over the past 3 years and their commitment to high-quality manufacturing, allied to timely delivery, makes them an ideal manufacturing partner for Adaptimmune. This arrangement will complement well our new manufacturing plant currently under construction in Philadelphia."

FATE COLLABORATES WITH MSKCC FOR OFF-THE-SHELF T-CELL IMMUNOTHERAPIES

Fate Therapeutics, a San Diego-based biopharmaceutical company specialized in the development of cellular immunotherapies for cancer and immune disorders, has announced a strategic agreement with MSKCC for the development of off-the-shelf T-cell product candidates using engineered pluripotent cell lines.

This 3-year research and development collaboration will be led by Dr Michel Sadelain, Director of the Center for Cell Engineering and the Stephen and Barbara Friedman Chair at MSKCC. The collaboration aims to unite research, preclinical development and manufacturing works currently being conducted independently at Fate and MSKCC to accelerate the clinical translation of T-cell product candidates derived from engineered pluripotent cells.

Together, the groups will have significant experience and expertise necessary to deliver off-the-shelf T-cell immunotherapies, including the engineering, maintenance and expansion of induced pluripotent cell lines and the scalable generation of T cells with enhanced safety profiles and effector functions.

Under the terms of the agreement, Fate Therapeutics will have the exclusive license of the intellectual property covering induced pluripotent cell-derived immune cells, including T cells and NK cells. In addition, Fate also has the option to exclusively license intellectual property arising from all research and development activities under the collaboration.

Fate has also launched a new venture company, Tfinity Therapeutics, which will focus on the advancement of off-the-shelf T-cell

immunotherapies using Fate's patent-protected pluripotent cell platform. Fate's portfolio consists of over 60 issued patents and 90 pending patent applications, which cover compositions and methods critical for deriving, engineering, maintaining and differentiating induced pluripotent cells.

Scott Wolchko, President and CEO of Fate Therapeutics, commented: "This partnership brings together Memorial Sloan Kettering's excellence in the manufacture and delivery of cell-based immunotherapies, and our established expertise in pluripotent cell generation, engineering and differentiation. Together, we are at the forefront of an off-the-shelf paradigm shift, seeking to broaden patient access to revolutionary T-cell immunotherapies through a renewable, robust and standardized product approach."

RETROSENSE COLLABORATES WITH UCSD TO ADVANCE OPTOGENETICS

RetroSense Therapeutics, a US-based biopharmaceutical company focused on the development of gene therapies for retinal degenerative diseases, has signed a global license agreement with the University of California, San Diego (UCSD) to develop red activatable channelrhodopsin (ReaChR), a next-generation optogene developed by the late Nobel Laureate Dr Roger Y Tsien.

The company is currently developing its optogenetic-based lead candidate RST-001 for the treatment of retinitis pigmentosa (RP) and advanced dry age-related macular degeneration and is currently in a Phase 1/2a trial. This ongoing trial is designed as an open-label, dose-escalation study to determine the safety and tolerability of unioocular intravitreal injection of RST-001 in patients with RP. Intravitreal administration of RST-001 delivers a photo switch, channelrhodopsin-2, to cells in the retina of the eye. When expressed, the channelrhodopsin-2 protein depolarizes in response to light thus generating a signal that is transmitted to the brain.

Sean Ainsworth, CEO of RetroSense Therapeutics, commented: "The ReaChR license allows us to continue building on our world-leading platform in optogenetics for vision restoration. Because the ReaChR opsin is red-shifted, it complements our existing development programs quite nicely, expanding our spectrum."

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

Juno Therapeutics, a Seattle-based biopharmaceutical company specialized in the development of cell-based cancer immunotherapies, has entered into an exclusive license agreement with Memorial Sloan Kettering Cancer Center (MSKCC) and Eureka Therapeutics for

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the development of chimeric antigen receptor (CAR) cell therapies for patients with multiple myeloma. B-cell maturation antigen (BCMA), the primary target used for the development of CAR was developed under a collaboration agreement between Eureka Therapeutics and MSKCC. The parties expect the BCMA CAR to enter clinical trials in early 2017. The financial terms of the agreement are not disclosed yet.

Dr Hy Levitsky, the CSO of Juno, commented: "We are optimistic that CAR-T therapy can be an important component in treating patients with multiple myeloma, and we are pleased to bring additional fully-human binding domains against BCMA and other targets into our program. We believe that a multi-pronged approach may be necessary to treat multiple myeloma, and we will pursue more than one target against myeloma. The MSK and Eureka constructs are promising additions to our portfolio that will accelerate our efforts and provide additional opportunities to combat this disease."

KITE ENTER LICENSE AGREEMENT WITH NIH

Kite Pharma, a clinical-stage biopharmaceutical company, has announced that it has entered into an exclusive, global license agreement with the National Institutes of Health (NIH), to advance the development of T-cell receptor (TCR)-based product candidates for the treatment of tumors expressing mutated KRAS antigens. The company expects its first licensed KRAS product candidate to enter clinical trial in 2016.

Under the terms of the agreement, Kite will make an upfront payment to NIH and the latter is also eligible to receive other milestone payments and royalties on products covered by the license.

Dr Arie Belldegrun, Kite's Chairman, President and CEO, commented: "Kite has taken an important step toward building the first therapeutic franchise of its kind for cancers driven by KRAS mutations and has further expanded its efforts in building a TCR portfolio across key classes of antigens."

FULCRUM PARTNERS WITH HORIZON TO DEVELOP CRISPR-BASED THERAPIES

Fulcrum Therapeutics, a Cambridge, MA-based biotechnology company focusing on the development of therapeutics based on modulating gene expression, has announced its partnership with the UK's Horizon Discovery to advance CRISPR's use in the treatment of genetic diseases.

Under the terms of the agreement, Horizon will apply its CRISPR platform to identify gene

regulation targets for Fulcrum, for the development of next-generation therapies. Through this partnership, Horizon Discovery Group aims to become a major player in gene editing technologies. The program, which is expected to run between 5 and 7 months, will initially focus on genetic diseases where no effective treatment options currently exist. Fulcrum is currently engaged in early-stage work on two monogenic diseases: Fragile X syndrome and a form of muscular dystrophy called facioscapulohumeral muscular dystrophy.

Robert Gould, president and CEO of Fulcrum Therapeutics, commented: "Horizon's reputation in gene editing and its applications, including CRISPR-based screening, is unparalleled. It was natural for Fulcrum to turn to Horizon as a long-term partner. With their deep scientific expertise, and with a broad IP portfolio underpinning their work, we are confident in a productive and exciting collaboration."

LIONS SIGNS AGREEMENT WITH POLYBIOCEPT AB TO ADVANCE TIL-BASED CANCER THERAPEUTICS

Lion Biotechnologies, a clinical-stage biopharmaceutical company specialized in the development of tumor-infiltrating lymphocyte (TIL)-based cancer immunotherapies, has entered into a license agreement with Sweden-based PolyBioCept AB and a clinical trials agreement with the Karolinska University Hospital to advance TIL-based therapeutics for multiple cancer indications.

Under the terms of the agreement, Lion will have exclusive worldwide rights to two international patent applications related to a specific combination of cytokines used for the enrichment of TIL products. Along with PolyBioCept, Lion also holds co-exclusive worldwide rights to make genetically engineered TIL using the cytokine cocktail for use in multiple cancer indications. Under the terms of the clinical trials agreement, the Karolinska University Hospital will conduct two clinical studies in glioblastoma and pancreatic cancer using these engineered TILs.

PolyBioCept will receive an upfront fee of $2.5 million from Lion under the exclusive license and is also eligible for additional payments upon achievement of certain clinical, regulatory and sales milestones. In addition, Lion will also pay a total of $1.7 million to the Karolinska University Hospital and PolyBioCept to conduct the clinical trials in glioblastoma and pancreatic cancer.

Dr Maria Fardis, CEO of Lion Biotechnologies, commented: "We are excited to be working with PolyBioCept and the Karolinska University Hospital to treat glioblastoma and pancreatic cancer patients with TIL manufactured with a new combination of cytokines developed by researchers at the Karolinska Institute. Our partnership with Karolinska further positions Lion to be a leader in developing cell-based immunotherapies that can treat solid tumor indications."

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BRAINVECTIS RAISES FUND FOR GENE THERAPY OF AD & HD

BrainVectis, a France-based biotechnology company specialized in the development of gene therapy for neurodegenerative diseases, has announced that it has raised €1 million ($1.1 million) from private investors in a Series A financing.

A spin-off of INSERM, the company will use the funds to complete preclinical pharmacological tests to initiate its gene therapy clinical trials, in 2019 for Huntington's disease and in 2021 for Alzheimer's disease. The fundraising campaign was supported by Cassagne et Associés and Guillaume Rémy (Velvet Avocats).

BrainVectis's initial two clinical programs are aimed to stopping the progression of Alzheimer's and Huntington's diseases by restoring cholesterol metabolism in the brain. Reduction in the expression of CYP46A1, a key enzyme in cholesterol metabolism, is a hallmark of these neurodegenerative diseases. BrainVectis plans to use gene therapy to restore the expression of this protein in the brain of patients.

The company has an exclusive license to use the INSERM patents behind the innovative therapy. The company was created with the support of the Technology Transfer Acceleration Company (SATT) IDF Innov through the financing of complementary proof of concept studies and the Paris Biotech Santé incubator and has collaboration with the French Alternative Energies and Atomic Energy Commission (CEA).

Dr Nathalie Cartier-Lacave, founder of BrainVectis, commented: "We are extremely grateful for the support of Paris Biotech Santé and the SATT IDF Innov who have helped us to create the company and given us an exclusive license for the patents required to develop the project." Dr Cartier-Lacave is a research physician specialized in gene therapy, the director of research at INSERM and the president of the European Society of Gene and Cell Therapy.

ALLERGAN BUYS GENE THERAPY START-UP RETROSENSE THERAPEUTICS

Allergan has bought gene therapy start-up RetroSense Therapeutics, gaining access to an early clinical candidate to treat RP. Allergan has paid RetroSense a $60 million upfront payment, and has agreed to potential regulatory and commercialization milestone payments related to its lead development program, RST-001.

David Nicholson, Allergan's chief R&D officer, commented: "The RST-001 program and its optogenetic gene therapy approach could be a real breakthrough in the treatment of unmet needs across a host of retinal conditions, including RP. The team at Allergan is excited by the prospect of advancing an entirely new approach in the treatment of retinal diseases, and this technology is highly complementary to our ongoing development programs in this critical treatment area."

EXPERT PICK

Allergan's investment in RetroSense Therapeutics provides further momentum to the ocular gene therapy space and also bolsters its already substantial presence in ophthalmic treatments. The approach taken by RetroSense is distinct from other players in the retinitis pigmentosa field. Rather than targeting a specific gene mutation (of which there are at least 50 in RP), RetroSense has developed a therapeutic approach that confers light sensitivity to cells that were not previously, or natively, light sensitive; this has the potential to allow the treatment to be used in all patients with RP rather than subsets, and also holds a more distant promise of treatment for age-related macular degeneration. RST-001 is now in a Phase 1/2a clinical trial in adult patients with advanced RP, with first data due in mid-2017; it will be fascinating to see whether any hints of efficacy emerge from this first clinical trial. – Richard Philipson

CRISPR THERAPEUTICS DECIDES TO GO PUBLIC

Switzerland-based gene editing company CRISPR Therapeutics has disclosed plans to raise up to $90 million in an initial public offering (IPO), in the latest sign of growing interest in gene editing technology to fix faulty genes. The company plans to list under the ticker $CRSP on the Nasdaq.

CRISPR Therapeutics is specialized in the development of gene-based therapeutics for life-threatening diseases using its proprietary CRISPR/Cas9 gene-editing platform. The company has licensed its CRISPR/Cas9 patent estate for human therapeutic use from its scientific founder, Dr Emmanuelle Charpentier. CRISPR applies its gene editing technology to cure beta-thalassemia, sickle cell disease, Duchenne muscular dystrophy and cystic fibrosis. Although it is headquartered in Basel (Switzerland), its R&D operations are based in Cambridge, Massachusetts.

CRISPR is the third gene editing company that has decided to go public. Its two Cambridge-based rivals, Editas Medicine and Intellia Therapeutics, had raised $94.4 million and $108 million, respectively, earlier this year.

However, the question remains whether CRISPR can perform better on the stock market than Editas and Intellia. Shares of Editas have only gained 3% in the past 7 months from the IPO price, while those of Intellia have increased 17% in the past 4 months. The volatility of other companies in the field might hinder CRISPR in the coming months.

In its SEC filing, CRISPR says: "We believe that our scientific expertise, together with our gene editing approach, may enable an entirely new class of highly active and potentially curative treatments for patients for whom current biopharmaceutical approaches have had limited success."

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THERMO FISHER SCIENTIFIC EXPANDS SERVICE TO CLINICAL TRIALS IN JAPAN

Thermo Fisher Scientific, a global company headquartered in the USA specialized in the development of products related to the biotechnology industry, has announced the expansion of its Fisher BioServices cryogenic service capabilities in Japan. With this latest expansion, the company aims to become a major service provider to the cell and gene therapy industry by enabling clinical trials to be conducted across multiple locations around the world.

Fisher BioServices holds expertise and industry-compliant resources to support its customers on their path towards commercialization. Its initial facility in Tokyo was expanded to incorporate cryogenic storage and logistic facilities for the cell and gene therapy industry. The company is planning to use this approach to configure and replicate each site to meet the specific requirements of individual clinical trials with minimal variation, regardless of the volume or geographic location.

ALNYLAM OPENS EU HUB IN THE UK

Alnylam has announced the opening of its new development & commercial hub in Maidenhead, UK.

The news about Alnylam's decision has slightly eased the concerns of overseas pharmaceutical companies about Britain's attractiveness in the wake of the EU referendum. In anticipation of substantial growth over the next 5 years, Alnylam is opening its office in Maidenhead with a core Clinical Development, Regulatory Affairs and Commercial team and space for an additional 100 employees.

Akshay Vaishnaw, CMO of Alnylam, commented: "Since our inception in 2002, Alnylam has pioneered new and innovative potential treatments for challenging diseases. We're thrilled to be expanding our global presence in the UK and Maidenhead in particular. This important new office will play a critical role in advancing our cutting-edge investigational RNAi therapies toward regulatory approval and launch in European markets to benefit patients with life-threatening diseases as quickly as possible."

Alnylam's pipeline of investigational RNAi therapeutics is focused in three therapeutic areas and includes genetic medicines for the treatment of rare diseases, cardio-metabolic diseases and hepatic infectious diseases. By the end of 2020, Alnylam expects to achieve a company profile with three marketed products and 10 RNAi-based therapeutic clinical programs. The company has license collaborations with leading pharmaceutical companies including Ionis, Novartis, Roche, Takeda, Merck and Sanofi Genzyme.

Brendan Martin, General Manager of Alnylam for the UK and Ireland, commented: "With its strong academic and clinical research sector, as well as its universal health service and regulatory bodies constantly striving to be more streamlined and efficient, the UK has a lot to offer as a development hub for innovative medicines. Our investment here signals a trust that the UK community will continue to treat this mission with the urgency and importance it deserves."