Commercial insight: cell and gene therapy

MAY 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: This month sees several companies release positive news at the *American Society of Gene and Cell Therapy (ASGCT) 20th Annual Meeting*. Agilis Biotherapeutics (MA, USA), Solid Biosciences (MA, USA) and Intellia Therapeutics (MA, USA) all presented data showing advancement of their programs, and it's good to see 5-year follow-up data from Agilis showing evidence of persistent clinical benefit in patients with AADC deficiency treated with a single dose of the CNS-delivered, AAV-based therapy. On the regulatory front, Spark Therapeutics (PA, USA) has completed its rolling BLA submission and two products – Xylocor's (PA, USA) angiogenesis gene therapy for chronic, refractory angina and Sangamo's (Canada) cDNA gene therapy for haemophilia A – have received fast track designation from FDA. Finally, news from Editas Medicine (CA, USA) that the planned IND for its CRISPR-based Leber congenital amaurosis treatment is delayed by at least 6 months shows the vulnerability of companies to challenges in manufacturing gene therapies.

GENE THERAPY
Richard Philipson
Chief Medical Officer,
Trizell Ltd, UK

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

CELL THERAPY: Asterias provided an update this month on progress in its SCiStar study investigating embryonic stem cell-derived oligodendrocyte progenitors (AST-OPC1) in patients with spinal cord injury. Several months ago the company reported on positive clinical benefit to patients through improved motor function. New data generated by magnetic resonance imaging shows that patients who received AST-OPC1 cells did not form lesion cavities in their spinal columns. Lesions, which typically fill with liquid, prevent recovery of motor and sensory function. This is a significant milestone in the development of treatments for spinal cord injury because it provides a mechanism for spinal cord recovery that directly results from engraftment of cells into the spine.

ISCO COMPLETES NEURAL CELL TRANSPLANTATION IN PD PATIENTS

The California-based biotech company, International Stem Cell Corporation (ISCO), has successfully completed ISC-hpNSC® neural cell transplantation in its first cohort of Parkinson's disease patients for their Phase 1 clinical study.

ISCO is developing human parthenogenetic neural stem cells (hpNSCs) with the hope of treating a range of neurological conditions. This initial Phase 1 trial is assessing the dose escalation and preliminary efficacy of transplanting the neural stem cells, which have been derived from human parthenogenetic stem cells, in subjects with moderate Parkinson's disease. The trial conducted at the Royal Melbourne Hospital in Australia will test three dose regimens between 30,000 and 70,000 ISC-hpNSC® cells injected intracerebrally into the striatum and substantia nigra of patients with Parkinson's disease. The recent update is a positive start for the trial, with no patients experiencing adverse events and all of the transplantation operations going according to plan.

The death of dopaminergic neurons is the cause of the motor symptoms associated with Parkinson's disease. The transplantation of pure neural cells therefore has the potential to provide neurotrophic support and neuroregeneration to the affected tissues of the recipient brain. This would be a first in the efforts to treat the disease as no current approaches target the restoration of the damaged dopaminergic neurons. Preclinical studies of ISC-hpNSC® in rodents and non-human primates have shown improvement in Parkinson's disease symptoms and increase in brain dopamine levels following the intracranial administration of the therapy. A further plus found in preclinical models was the absence of adverse events such as dyskinesia, system toxicity or tumors.

Russell Kern, executive VP and CSO of ISCO, commented: "We look forward to dosing our second cohort with 50 million cells and enrolling the rest of our clinical trial participants in 2017. The Data Safety Monitor Board meeting will be held in the beginning of May and we expect to receive approval

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SOLID'S SGT-001 BACKED BY PRECLINICAL DATA AS A DMD TREATMENT APPROACH

SGT-001, the investigational microdystrophin gene therapy from Solid Biosciences, has been proved to sustain significant microdystrophin expression and improvements in muscle function during preclinical trialling. Intended to treat Duchenne muscular dystrophy (DMD), the work has been carried out in collaboration with researchers at the University of Missouri and Texas A&M University.

DMD is a muscular degeneration disease characterized by a lack of dystrophin. Solid's lead candidate SGT-001 therefore aims to initiate transgene expression throughout the body in order to produce microdystrophin. The therapy is adeno-associated viral (AAV) vector-mediated. These latest results come from canine subjects in an ongoing, long-term and dose-ranging study.

Correlations were observed between the animals treated and those with sustained transgene expression and significantly improved muscular function. Transgene expression was found to be dose dependent and four dose regimens were able to achieve this end. The longest lasting results reached up to 24 months from administration.

The full extent of the data was presented at the American Society of Gene and Cell Therapy (ASGCT) 20th Annual Meeting. As part of Solid's investigational new drug (IND) enabling research program, the company hopes that this data will pave the way for safety and efficacy clinical trialling of SGT-001.

VP Joel Schneider commented, "These preclinical data show the potential efficacy, durability and tolerability of SGT-001, and give us further confidence in our plan to initiate our clinical program later this year."

PRIORITY REVIEW FOR KITE'S KTE-C19 IN THE NEXT LEG OF THE CAR-T RACE

The latest news in the CAR-T race to market sees Kite Pharma being granted priority review for their autologous therapy KTE-C19, also known as axicabtagene ciloleucel. This brings the approval date for the drug forward to November this year, two months shy of rival Novartis' imminent September Prescription Drug User Fee Act (PDUFA) date.

Kite's investigational therapy is designed to express CARs on the surface of a patient's own T cells. These target CD19, a receptor expressed on B-cell lymphoma and leukemia cells, and thus redirect T cells to kill the cancer cells. KTE-C19 has been granted breakthrough designation to treat diffuse large B-cell lymphoma (DLBCL),

transformed follicular lymphoma and primary mediastinal B-cell lymphoma. Kite's Biologics License Application (BLA), which is under review, was supported by data from their Phase 2 trial, ZUMA-1, that demonstrated a significant objective response rate to the therapy of 88%.

Whilst both companies have had breakthroughs with DLBCL, competitor Novartis is seeking approval for a different indication; B-cell acute lymphoblastic leukemia (ALL) in kids and young adults. This means that despite the race to market, the two therapies are not likely to initially clash directly.

Kite's Chief Medical Officer, David Chang, said of the news: "Patients with refractory aggressive NHL face a dire prognosis with only a 50% chance of surviving 6 months. This underscores the urgent medical need for these patients and why every day matters, from development to manufacturing to clinical experience."

The next significant announcement from the CAR T race is expected mid-June, when Novartis unveils the results from its Juliet trial at a conference in Switzerland.

5-YEAR FOLLOW-UP DATA OF GENE THERAPY TREATMENT FOR AADC DEFICIENCY

Five years ago, Dr Paul Hwu, professor at the National Taiwan University Hospital, treated 18 patients with AGIL-AADC in an Agilis Biotherapeutics' trial for which he was the principal investigator. This gene therapy was designed to target the rare disease aromatic L-amino acid decarboxylase (AADC) deficiency, and in one of the longest follow-up periods reported in the gene therapy industry, results to date have now been announced.

The enzyme AADC is responsible for the final step in the synthesis of key neurotransmitters dopamine and serotonin. The deficiency is debilitating and results in developmental failure, global muscular hypotonia and the need for lifelong care amongst a plethora of symptoms. AGIL-AADC is Agilis Biotherapeutics' lead candidate and comprises of an adeno-associated virus (AAV) vector containing the human gene for the AADC enzyme.

The 5-year results reveal significant improvements, measured by the well-established Peabody Development Motor Scale, Second Edition (PDMS-2) and the Alberta Infant Motor Scale (AIMS), in motor function and the achievement of motor development milestones. Patients also showed de novo dopamine production as visualized by F-DOPA PET imaging, and the emergence of dopamine metabolites. Together, these results represent considerable improvements for the treated subjects over the period following the initial single dose treatment.

Agilis' CMO, Kirsten Gruis, commented that the data reinforces the premise that "gene therapy may

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be able to provide durable benefits to patients with debilitating disorders that affect the central nervous system." Dr Hwu added, "We have seen important treatment benefits as well as a good safety and tolerability profile to date. AADC deficiency patients treated with AGIL-AADC have exhibited improvements across multiple functional scales, developmental milestones, biomarkers and imaging measures."

PROMISING DATA FROM MAGENTA'S CORD BLOOD EXPANSION TRIAL

New data supporting further testing of Magenta Therapeutic's Stem Regenin-1 as part of their lead expansion program, MGTA-456, has been released. The results have been collected from three clinical trials with 36 enrolled patients to test the expansion of umbilical cord blood stem cells in various settings.

MGTA-456 aims to expand the number of cord blood stem cells used in transplants to achieve superior clinical outcomes compared to standard transplant procedures. These latest results revealed a >300-fold increase in the number of $CD34^+$ hematopoietic progenitors. Also found in the trials were significantly quicker engraftment times and improved platelet recovery.

The Massachusetts-based company have presented their latest findings at the *American Society of Gene and Cell Therapy (ASCGT) Annual Meeting* in Washington.

FAST TRACK DESIGNATION FOR XYLOCOR'S ANGIOGENESIS GENE THERAPY

A gene therapy approach to treat chronic, refractory angina has received Fast Track designation from the US Food and Drug Administration (FDA). The therapy, XC001, is the lead candidate of biotech company XyloCor Therapeutics.

A one-time treatment, XC001 promotes angiogenesis, the formation of new vessels that can provide arterial blood flow to myocardial regions with inadequate blood supply. Increasing myocardial blood flow has the potential to relieve myocardial ischemia, increase left ventricular performance, alleviate pain symptoms and disability, and improve prognosis.

The intended recipients are those refractory to standard medical therapy and not amenable to conventional revascularization procedures such as coronary artery bypass surgery and percutaneous coronary intervention and stents. The fast track designation expedites the regulatory process for the drug, with the hope of streamlining its road to market and hence

to these patients for whom it is a sole treatment option.

Upon sufficient funding, XyloCor anticipates the initiation of clinical trials. CEO Al Gianchetti commented, "Achieving Fast Track status validates the need for XC001, which has the potential to be a unique treatment for this serious condition with high unmet need – chronic, refractory angina." Magnus Ohman, a professor at Duke University, also commented on the news: "These patients have significant limitations in terms of their daily activities because of the chest pain associated with their ischemic disease and XC001 could be an important new option for them."

RMAT DESIGNATION FOR VERICEL'S MSC HEART THERAPY

The FDA has granted Vericel Corporation Regenerative Medicine Advanced Therapy (RMAT) designation to the company's investigational therapy, ixmyelocel T. An autologous multicellular expanded therapy, ixmyelocel T is intended to treat advanced heart failure due to ischemic dilated cardiomyopathy. The drug already holds Orphan designation from the FDA.

The RMAT designation expedites the development and review process for regenerative therapies for serious or life-threatening conditions. A drug must be supported by preliminary clinical evidence, which indicates the potential to address an unmet need in order to be granted the designation. In the case of ixmyelocel T, this evidence came from Vericel's Phase 2b ixCELL-DCM clinical study which resulted in a 37% reduction in deaths and hospitalizations; successfully meeting the trial's primary endpoint. The significance of the results was such that patients who received a placebo in the double blind trial have now been offered the option to receive ixmyelocel T.

Dilated cardiomyopathy is a condition that is characterized by a weakening of the heart muscle and enlargement of the heart chambers. Vericel's ixmyelocel T is manufactured by selectively expanding a population of mesenchymal stem cells and alternatively activated macrophages from the patient's own bone marrow. These treat dilated cardiomyopathy via anti-inflammatory and pro-angiogenic factors known to be important for repair of damaged tissue.

"Being among the first products to receive the RMAT designation, in addition to the recently granted Fast Track designation, highlights both the significance of the results from the ixmyelocel T Phase 2b ixCELL-DCM clinical study and the unmet medical need for improved therapies to treat advanced heart failure due to ischemic dilated cardiomyopathy," stated Nick Colangelo, Vericel President and CEO.

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Vericel joins a small but growing list of companies that have received a Regenerative Medicine Advanced Therapies (RMAT) designation. The FDA granted Vericel the designation for Ixmyelocel-T for the treatment of advanced heart failure. The RMAT designation, part of the 21st Century Cures Act, is granted to a company if there is early evidence that a therapy may be able to cure or reverse a serious, or life-threatening condition. Benefits of the designation include earlier engagement with the FDA, accelerated approval pathways, approval based on surrogate or intermediate endpoints predictive of long-term benefit, and the opportunity to use patient registries and other real-world evidence to deliver on post-approval requirements. – Mark Curtis

BLA SUBMITTED FOR SPARK'S VORETIGENE NEPARVOVEC

The FDA has 60 days to determine the completeness of Spark Therapeutics' Biologics License Agreement (BLA), completed this month for its gene therapy candidate voretigene neparvovec.

Voretigene neparvovec is a one-time gene therapy for the treatment of patients with vision loss due to biallelic RPE65 mutation-associated retinal disease. The therapy has completed a Phase 3 trial, which enrolled 41 patients, evidence from this was included in the BLA submission along with two other clinical trials. Results included were measured by mobility testing scores, visual acuity testing and full-field light sensitivity threshold testing for white light.

If all goes to plan with this latest BLA filing, the review period for the therapy will be initiated shortly. CEO Jeffrey Marrazzo commented, "Completion of the rolling BLA is another step forward in our goal to bring this investigational gene therapy to people living with RPE65-mediated IRD who currently have no approved pharmacologic treatment options."

The announcement from Spark Therapeutics (PA, USA) that the company has completed its rolling submission of a Biologics License Application (BLA) for voretigene neparvovec marks an important milestone for the development of this AAV-based treatment for RPE65-mediated inherited retinal disease. RPE65, which was first described in 1993, plays a critical role in the visual cycle in retinal pigment epithelial cells; mutations in RPE65 account for approximately 2% of cases of recessive retinitis pigmentosa and approximately 16% of cases of Leber's congenital amaurosis. So, whilst the population of patients that could benefit from this treatment is extremely small, the response of FDA to the application, based on a limited dataset of only 41 patients, could prove to be an important bellwether for the field. – Richard Philipson

PROMISING NEW MRI DATA FROM ASTERIAS' SCISTAR TRIAL

New serial magnetic resonance imaging (MRI) scans from Asterias Biotherpeutics' ongoing AST-OPC1 SCiStar Phase 1/2a clinical trial in patients with severe spinal cord injury indicate successful engraftment of AST-OPC1 cells, along with the prevention of lesion cavity formation.

AST-OPC1 is an oligodendrocyte progenitor population derived from human embryonic stem cells. The cells are thought to have reparative functions that address the complex pathologies at the site of spinal cord injuries. These include the production of neurotrophic factors, stimulation of vascularization, and induction of remyelination of denuded axons, which are all vital for the sustenance of nerve impulses at an injury site. The cells are being trialled in a dose escalation Phase 1/2 trial, SCiStar, from which these latest results have arrived.

When a person suffers a severe spinal injury, fluid-filled lesion cavities typically form after 3 months and significantly hinder the recovery of motor and sensory functions. Asterias' MRI data is therefore very promising as candidates treated with both high (10 million cells) and low (2 million cells) doses indicated no signs of lesion formation at 12 months follow-up. The patients who have taken part in the study are characterized by a loss of movement below their injury sites and severe paralysis of the upper and lower limbs. It is hoped that successful engraftment of the AST-OPC1 cells will prevent cavitation, a process which results in loss of motor and sensory function as well as secondary conditions.

CMO Edward Wirth commented, "These new follow-up results based on MRI scans are very encouraging, and strongly suggest that AST-OPC1 cells have engrafted in these patients post-implantation and have the potential to prevent lesion cavity formation, possibly reducing long-term spinal cord tissue deterioration after spinal cord injury."

NEW ANIMAL DATA FROM INTELLIA'S CRISPR CANDIDATE

Intellia therapeutics has presented its latest dataset at the American Society of Gene & Cell Therapy's Annual Meeting (ASGCT) in Washington, DC. The Massachusetts-based company reported the successful long-term suppression of a gene using its gene-editing CRISPR/Cas9 platform.

The target gene was the sequence coding for serum transthyretin (TTR) protein, mutations of which are associated with a host of amyloid diseases. Intellia's previous studies had shown a 97% reduction in TTR, driven by 70% gene editing efficiency working in mouse livers. The latest data corroborated these results, adding that the effects lasted for up to 6 months following a single, initial dose. A second study in rat livers revealed 66% gene editing,

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and up to 91% reduction in serum TTR protein levels, again following a single intravenous infusion. Crucially the results supported earlier data showing that the CRISPR drug is rapidly cleared from the body, thus reducing the chances of off-target effects that could cause toxicity.

Intellia is one of a number of companies hoping to follow in the footsteps of Chinese scientists, who last year treated adult cancer patients with CRISPR modified cells. Amongst those in the race to market are Editas and CRISPR Therapeutics. For Intellia, the next hurdle is expanding its findings to non-rodent species as the FDA generally requires evidence from two species, one of which a non-rodent species, before it can progress into clinical studies. The company's projected timeline sees approval of human trials in early 2018.

Senior VP David Morrissey commented that the rat study "validates the in vivo CRISPR/Cas9 platform using Intellia's proprietary LNP delivery system," adding that it shows "the ability to expand out studies in larger species."

Intellia Therapeutics has taken another step toward human trials in transthyretin (TTR) amyloidosis using its CRISPR/Cas9 gene editing technology after reporting new data from mouse and rat models. 6-month follow-up data from the mouse model demonstrated both durability and high editing efficiency in vivo; the technology was further validated in the rat model following single intravenous administration, with robust, dose-responsive lipid nanoparticle-mediated editing of the TTR gene in rat livers. TTR amyloidosis is a rare, slowly progressive condition characterized by the build-up of the protein amyloid in organs and tissues, most frequently the peripheral and central nervous systems and heart. A number of different therapeutic approaches are already in clinical development, with Ionis Therapeutics recently announcing that its Phase 3 NEURO-TTR study of the antisense oligonucleotide inotersen in patients with familial amyloid polyneuropathy (FAP) met both primary endpoints. – Richard Philipson

FAST TRACK DESIGNATION FOR SANGAMO'S HEMOPHILIA A SB-525

California based Sangamo Therapeutics has received Fast Track designation from the FDA for their Hemophilia A therapy candidate, SB-525. The therapy is being developed in collaboration with Pfizer as part of an exclusive global agreement.

Hemophilia A is a monogenic rare bleeding disorder that is characterized by mutations in the F8 gene, which encodes Factor VIII clotting protein. Thus symptoms of the disorder include bleeding episodes after injuries, and spontaneously. Secondary symptoms include joint diseases such as arthritis.

Sangamo's SB-525 targets the mutation by delivering a human Factor VIII cDNA construct and proprietary, synthetic liver

specific promoter to liver cells via a recombinant adeno-associated virus (AAV) vector. A single treatment is intended to sustain the therapeutic expression of Factor VIII protein. Enrolment for Phase 1/ 2 trialling of SB-525 is expected to start later this year. The candidate has previously been designated as an orphan drug as well as having an Investigational New Drug application cleared.

It is hoped that the fast track designation will truncate the time to drug approval as SB-525 is deemed to fit an unmet medical need and therefore will benefit from an expedited review process and frequent communication with the FDA.

LICENSING AGREEMENT SIGNED BETWEEN POSEIDA & TENEOBIO

Teneobio and Poseida Therapeutics have signed a commercial license agreement to enable the use of Teneobio's UniDabs™, single-domain, human heavy chain only antibodies in Poseida's proprietary CAR T-cell therapy programs. Under the terms of the agreement, Tenebio will receive an upfront payment, potential clinical milestones and royalties on commercial sales.

Poseida is currently developing CAR T cell immunotherapies to target multiple myeloma and other cancer types. Versatile antibody variable domains (UniDabs™) derived from UniAbs™ can be assembled into multi-specific and multivalent therapeutic proteins. It is intended that these will be integrated with Poseida's gene editing capabilities to maximize the efficacy of the company's gene therapies.

Wim van Schooten, CSO of Teneobio, commented "this agreement further validates the utility of UniDabs™ in CAR T-cell therapy. In the last year, we have made excellent progress in identifying and advancing UniAbs™, best-in-class human heavy chain only antibodies from our proprietary UniRat® transgenic platform, for bi- and multi-specific antibody therapeutics with great manufacturability. Ultimately, the greater specificity of bi- and multivalent CARs will enable the pursuit of solid tumor CAR T-cell therapy."

GSK & BLUEBIRD BIO ENTER LENTIVIRAL LICENSE AGREEMENT

To propel the development and commercialization of gene therapies to treat the rare diseases Wiskott-Aldrich syndrome and metachromatic leukodystrophy, GlaxoSmithKline (GSK) has entered into a worldwide license agreement with bluebird bio for the use of the latter's proprietary lentiviral vector platform.

Under the agreement, GSK will non-exclusively license bluebird lentiviral technology patent rights in order to aid the development of their own gene therapies. The terms of the agreement included an upfront payment to bluebird bio, potential regulatory milestone payments and low single digit royalties

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on net sales of products sold as a result of the licensing.

Bluebird bio has been a leader in the field for lentiviral gene delivery, which it has used to develop a number of its own gene therapy programs targeting, for example, cerebral adrenoleukodystrophy, thalassemia and severe sickle cell disease.

"bluebird bio's work has been integral to the progress of lentiviral vector-based cell and gene therapy; over the past six years, we have taken the incredible potential of our lentiviral vector platform and successfully applied it to our own clinical gene therapy and oncology programs," said Chief Scientific Officer Philip Gregory. "We are pleased that our agreement with GSK now allows us to facilitate the work of others striving to develop transformational therapies for patients with rare genetic diseases."

TXCELL TO COLLABORATE WITH INSERM OVER CD8⁺ T DEVELOPMENT

In December 2016, the biotech company TxCell SA entered into a worldwide exclusive licensing agreement with Inserm Transfert a new subset of $CD8^+$ T reg cells developed at Inserm's laboratories. Now, the two companies along with the Nantes University have entered into an R&D collaboration agreement for the development of Chimeric Antigen Receptor (CAR) engineered $CD8^+$Treg cells (CAR-Tregs).

The Center for Research in Transplantation and Immunology (CRTI), an affiliate of both Inserm and Nantes University will work with TxCell to develop therapies targeting transplant rejection and autoimmune disease, particularly multiple sclerosis. A further aim is the inception of a manufacturing process to enable clinical proof-of-concept studies.

The move sees an extension of TxCell's research efforts; from $CD4^+$ cells to engineered $CD8^+$ Treg cells. The latter are considered non-cytotoxic and display a highly immunosuppressive mechanism of action.

Co-director of the CRTI team number 2, Dr Carole Guillonneau, commented, "This collaboration with TxCell will help us set in concrete the clinical development of innovative therapies based on CAR-CD8+Treg cells. We look forward to evaluating with TxCell the potential of these specific CAR-Tregs in the treatment of graft rejection and multiple sclerosis."

$41 MILLION KICKSTARTS BIOTECH VIVET THERAPEUTICS

With €37.5 million ($41 million) investment and Novartis, Sanofi and Gensight alumni on their executive team, Vivet Therapeutics is all set for a strong entrance into the gene therapy field. This initial funding round for the new, European company was led by Swiss giant

Novartis Venture Fund and Columbus Venture Partners with Roche Venture Fund, HealthCap, Kurma Partners and Ysios Capital also taking part.

Founded in Paris last year by Jens Kurth (formerly of Anokion and Novartis) and Jean-Philippe Combal (formerly of Gensight Biologics and Sanofi), Vivet Therapeutics also has a wholly owned subsidiary based in Spain. Collaborations with Fundación para la Investigación Médica Aplicada, a not-for-profit foundation at the Centro de Investigación Medica Aplicada; the University of Navarra based in Pamplona, Spain; and Massachusetts Eye and Ear Infirmary in Boston yielded the company's lead gene therapy program: VTX801.

VTX801 comprises of a modified adeno-associated virus vector, which carries a truncated version of the ATP7B gene. This is intended to treat Wilson disease, a rare genetic disorder caused by a defective gene in liver cells encoding the ATP7B protein. Effects of the deficiency include organ damage, neurologic symptoms and potentially death. Vivet's therapy will be applied to liver cells, and is thus projected to target the cause of the disease. It is towards developing this that Vivet's latest backing will go and the company expects to initiate the first in human trials for Wilson disease by the end of 2018.

The funds will also be used by Vivet to develop gene therapy programs for other rare and inherited metabolic diseases, including progressive familial intrahepatic cholestasis type 2 (PFIC2), progressive familial intrahepatic cholestasis type 3 (PFIC3) and citrullinemia type I.

CEO and co-founder Combal commented: "Vivet is delighted to have attracted such a substantial investment from these high-profile life sciences investors. This fundraising reflects our shared excitement about the potential of our lead candidate VTX801 and our technology for generating further novel gene therapies targeting rare inherited metabolic diseases. Early results from preclinical studies with VTX801 are very promising, and we are now well funded to advance this candidate into the clinic, while developing our portfolio and technologies." Human trialling of VTX801 is expected to begin in 2018.

$13.4 BARDA CONTRACT TO FUND CYTORI CELL THERAPY TRIAL

Cytori Therapeutics have executed a contract to the effect of $13.4 million with the Biomedical Advanced Research and Development Authority (BARDA), a division of the US Department of Health and Human Services, Office of the Assistant Secretary for Preparedness and Response (ASPR).

The funds will go towards the company's RELIEF trial, the next stage in the development of its supplemented Cytori Cell Therapy autologous skin graft for thermal burns. Preclinical data has indicated that intravenous delivery of Cytori Cell Therapy is associated with increased formation of new

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skin (epithelialization) and earlier restoration of the barrier function of the newly formed skin. This will be further investigated by the RELIEF trial in a clinical setting, with the primary endpoints of assessing safety and feasibility. The trial is approved to enroll up to 30 patients in up to ten US sites with study initiation expected to occur later this year. The patients will be those with thermal burn injuries covering between 20 and 50% of their body surface area.

BARDA is developing medical countermeasures for use following a mass casualty disaster involving burns. Cytori Cell Therapy is being developed as a potential treatment option that could be deployed in such a scenario owing in part to its cost effectiveness and potential acceleration of wound healing.

Cytori CEO Marc Hedrick has commented, "Cytori continues to develop Cytori Cell Therapy technology as a multiuse platform for use in both the routine clinical setting and in the event of a mass casualty emergency. There are several published reports indicating clinical benefit of Cytori Cell Therapy in chronic wound healing. This trial provides Cytori the opportunity to extend these reports by assessing utility of intravenous administration in an acute traumatic situation."

BARDA executed a $13.4M agreement with Cytori, bringing its total investment in the company's technology (DCCT-10) for thermal burn injury to $34.6 million. The funds from BARDA will be used for Cytori's US, pilot clinical study (RELIEF), investigating DCCT-10, an autologous, adipose-derived regenerative cell product, as an adjunct in patients who have burns to between 20 and 50% of the body and must receive an autologous skin graft. The product, which is administered systemically by IV, was shown to increase the rate of skin formation in preclinical studies. DCCT-10 is an interesting approach to treating thermal wounds, but future technologies will need to address the limitations imposed by autologous products, both in terms of the cell therapy and the skin graft. – Mark Curtis

$50 MILLION SERIES B FINANCING PROPELS MAGENTA THERAPEUTICS

Magenta therapeutics has finalized an oversubscribed Series B financing round that has raised $50 million to further the company's strategic vision. The round was led by GV with participation from all existing investors including Atlas Venture, Third Rock Ventures and Partners Innovation among others.

The financing will go towards fuel development of innovative product candidates with a focus on more precise preparation of patients, stem cell harvesting and stem cell expansion. Magenta CEO commented, "We aspire to accelerate products that could unleash the potential of transplantation to more patients,

including those with autoimmune diseases, genetic blood disorders and cancer. The resounding interest in Magenta from such a high-quality set of investors is a testament to our solid progress since launch, including building a world-class team and a robust pipeline, and generating promising early data."

Another contributor to the round was Be The Match BioTherapies, with whom Magenta has also entered into a collaboration deal with. Under the agreement, Magenta will be able to leverage Be The Match BioTherapies' capabilities, including its cell therapy delivery platform, industry relationships, clinical trial design and management, and patient outcomes data derived from the NMDP/Be The Match, which operates the largest and most diverse marrow registry in the world.

Be The Match president, Amy Ronneberg, said of their involvement with Magenta, "We are proud to have made our first equity investment as an organization in Magenta Therapeutics, and we share a vision to improve and advance the use of curative stem cell transplantation for patients with a wide range of diseases."

$10 MILLION TO FUND VIACYTE'S DIABETES STEM CELL THERAPIES

ViaCyte has bagged $10 million for the development of their stem cell-derived treatments for patients who have Type 1 diabetes and are at risk of complications. The funds will be used to initiate the clinical development of ViaCyte's PEC-Direct™ and PEC-Encap™, two stem cell candidates developed for the treatment of diabetes.

Participants in the financing included Asset Management Partners, W.L. Gore who recently partnered with ViaCyte to work on their Encaptra device, JDRF who established a $42 million fund for Type 1 diabetes research of late and some undisclosed investors.

The San Diego-based company's lead candidate, PEC-Direct is the intended beneficiary of the funds, which will go towards furthering its clinical development. The treatment works by administering stem cell-derived pancreatic progenitor cells in an implantable device. These cells are designed to mature into human pancreatic cells, including insulin-secreting beta cells. Targeted towards patients who experience severe hypoglycemic episodes, large fluctuations in blood glucose levels, or an inability to spot symptoms of low blood sugar, the treatment will be delivered alongside immune-suppressive drugs to prevent rejection.

The funds will also support ViaCyte's PEC-Encap, a stem cell-derived islet replacement therapy developed as a treatment for patients who require insulin to control their diabetes. It comprises of pancreatic progenitor cells in an immune-protective device called the Encaptra® Cell Delivery System. The Encaptra Cell Delivery System in addition to delivering the progenitor cells, also protects the cells from the host immune response, cutting the need for

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immunosuppression. PEC-Encap is currently being investigated in a Phase 1/2 trial in Type 1 diabetes patients.

"High-risk Type 1 diabetes has been successfully treated with cadaver islet transplants, but adoption of islet transplants has been limited, due in part to the insufficient supply of donor material," said ViaCyte CEO Paul Laikind, in a statement. "Because ViaCyte's PEC-01 cells are manufactured from pluripotent cells with unlimited proliferative potential, they can be made in vast numbers and therefore may be capable of solving the cell supply issue."

INDUSTRY VETERANS TO JOIN CASEBIA'S LEADERSHIP TEAM

The Massachusetts based venture, Casebia Therapeutics, has appointed three new members to its leadership team. Joint founded by Bayer and CRISPR Therapeutics, the company has been joined by **Ellen Ridge** as Senior Vice President of Operations; **Abraham Scaria** as Vice President of Ophthalmology; and in July, **Andrew M Scharenberg** as Chief Scientific Officer and Vice President of Hematology.

Casebia's focus is on harnessing CRISPR/Cas9 gene-editing technology to develop treatments targeting the areas of ophthalmology, non-malignant hematology, and autoimmune disease, followed by cardiovascular disease and hearing loss. It is hoped that the new roster of executives will bolster the ongoing research programs and bring candidates closer to trial.

On the appointments, CEO James Burns, stated: "Given our ambitious objectives, I am confident in these new executives' abilities to push this vital research and further scale our company in our quest to help patients."

New operations VP Ellen Ridge has previously worked at Intarcia Therapeutics and Genzyme. Her experience spans project management, enterprise risk and matrix management. Her academic record cites a BSc in Biology from the University of Massachusetts and an MBA from Bentley University.

Abraham Scaria has specialized in viral vectors and ocular gene therapy from over 20 years of work at Genzyme and Sanofi. He has a doctorate in biochemistry and molecular biology from Indiana University School of Medicine and will oversee Casebia's efforts to develop breakthrough therapies for inherited retinal diseases.

Currently an attending physician at Seattle Children's Hospital and Principal Investigator in the Center for Immunity and Immunotherapies at Seattle Children's Research Institute, Andrew M Scharenberg, will join Casebia shortly. Scharenberg also holds a number of academic positions and sits on the Transplantation Biology Consortium Program at Fred Hutchinson Cancer Research Center.