Commercial insight: cell and gene therapy

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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: Gene therapy is an approach that seems naturally suited to developing treatments for rare, monogenic diseases. This month sees progress for a much more prevalent condition – Alzheimer's disease – with encouraging preclinical data released by Sangamo Therapeutics using its ZFP technology. Another interesting announcement comes from Lysogene, which released baseline data from its observational study in MPS IIIA. Regulators have recently made clear their desire to see companies operating in rare diseases provide data on the natural history of the condition under study – Lysogene is clearly fulfilling the wishes of regulators in this regard. Not a month goes by without an announcement from bluebird bio, and this month is no different, with the announcement of positive data from the first patient treated with its lentiviral vector for severe sickle cell disease.

CELL THERAPY: It was a rollercoaster of a month for the CAR-T industry. At its low, Juno announced the discontinuation of its lead product JCAR015, a decision that, following a series of patient deaths and the halt of its Phase 2 ROCKET

study in 2016, is not entirely surprising. Juno will now focus on JCAR017, a product with a defined T-cell composition, and one it feels has better prospects for approval overall. While potential safety issues with CAR-T products have always been acknowledged, the news will test investor resilience. At its peak, later in the month, Kite Pharma announced completion of submission of its US Biologics License Application for axicabtagene ciloleucel in patients with relapsed or refractory aggressive NHL. Now we play the waiting game, for the approval of the world's first CAR-T product.

FDA FAST TRACK GRANTED TO MESOBLAST'S AGVHD THERAPY

Mesoblast limited, an Australia-based regenerative medicine company, has received Fast Track designation from the US Food and Drug Administration (FDA) for the use of its cell therapy, MSC-100-IV, in children with steroid refractory acute Graft Versus Host Disease (aGVHD). The Fast Track designation is intended to shorten the time to approval for the therapy through a priority review. Previous discussions with the FDA have established that MSC-100-IV is pitted to be a front-line therapy for the condition, and as such the development pathway has been streamlined as a route towards conditional approval.

The approval for Mesoblast's Fast Track application was hinged on clinical data from 241 steroid refractory aGVHD pediatric patients. Of these patients, 65% achieved overall response rate by day 28, a significant proportion of whom were surviving by day 100. A Phase 3 registration trial for MSC-100-IV is currently ongoing with 60 patients; recruitment is expected to be completed by mid-2017. Mesoblast believes that the success of this Phase 3 trial will be sufficient for conditional approval from the FDA.

As sections of the Biologics License Application for MSC-100-IV are completed, Mesoblast will be able to submit them for review as part of a rolling review process that is a feature of the Fast Track designation. Coupled with the product candidate's existing Orphan Indication status, and successful Phase 3 Trial outcomes, the Fast Track designation is likely to reap commercial benefits for the cell therapy once it reaches shelves, seemingly in the not too distant future.

LYSOGENE PRESENTS DATA OF ITS GENE THERAPY TRIAL FOR MPS IIIA

The gene therapy company Lysogene has announced baseline data from its Sanfilippo A Multinational Observational Study (SAMOS) at the 13th Annual WORLDSymposium™ in San Diego, California. Also known as Mucopolysaccharidosis Type IIIA (MPS IIIA),

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Sanfilippo A is a central nervous system disease in which the *SGSH* gene is missing. The study was designed to evaluate the clinical progression in untreated patients and will function as a non-concurrent control for the upcoming Phase 2/3 pivotal trial for Lysogene's MPS IIIA gene therapy candidate.

In the absence of a validated biomarker for MPS IIIA, SAMOS used a cognitive assessment and adaptive behaviour scale to track intellectual decline, hyperactivity and behaviour changes in 15 patients. A collaboration with the University of Minnesota (Shapiro *et al.*, 2015) has allowed Lysogene to perform metadata analysis on their results.

Lysogene's gene therapy candidate for MPS IIIA is a rAAV vector serotype rh.10 carrying the gene coding for *SGSH*. A healthy copy of the gene is to be delivered directly to the central nervous system in a one-time neurosurgical procedure. It is hoped that this will allow the body to permanently produce the missing enzyme; subsequently slowing or halting the progression of MPS IIIA.

Soraya Bekkali, CMO of Lysogene, commented: "We anticipate that this and forthcoming data will represent new learnings in this disease area and we know it will prove extremely valuable as Lysogene prepares for future pivotal studies in MPS IIIA".

THE GO AHEAD FROM FDA ON TIGENIX'S REVISED PHASE 3 STUDY

TiGenix NV has received positive feedback from the US Food and Drug Administration (FDA) on an improved protocol for its Cx601 global Phase 3 trial, for the treatment of complex perianal fistulas in Crohn's disease patients. Headquartered in Belgium, the company develops novel therapeutics from its proprietary platforms of allogenic or donor-derived stem cells. Ultimately, endorsement of the improved protocol is hoped to result in an earlier filing; a year earlier than originally planned.

TiGenix's European Phase 3 study of Cx601 (ADMIRE-CD) was the largest randomized study performed so far in Crohn's disease patients with complex perianal fistulas. Positive results from these prompted the company to submit a Marketing Authorization Application to the European Medicines Agency, and successively to approach the FDA with adjustments to the previously approved protocol for their global Phase 3 trial.

The amendments that the FDA has approved to the protocol include filing the Biologics License Application (BLA) on the basis of a 24-week, rather than 52-week, timeline. A broader target population and fewer participatory patients have also been approved. TiGenix continues to explore further expedited pathways to accelerate the submission and review process for its future BLA.

Cx601 is a suspension of allogeneic expanded adipose-derived stem cells. In 2009, it was granted Orphan Drug Designation by

the European Commission for the treatment of anal fistulas. Following a license agreement between TiGenix and Takeda in 2016, Takeda holds exclusive right to commercialize Cx601 for complex perianal fistulas in Crohn's patients outside of the USA.

TiGenix's product Cx601 may get to a marketing decision sooner than anticipated in the USA following some positive feedback from the FDA. The company was granted a Special Protocol Assessment from the FDA back in 2015, for the investigation of Cx601 to treat complex perianal fistulas in patients with Crohn's disease. As further positive data has continued to flow in from TiGenix's Phase 3 study in Europe, the FDA agreed that a BLA could be filed based on 24 weeks of patient follow-up versus 52 weeks; moving the technology forward in development by roughly 6 months. Further to this, the FDA agreed to a lower patient enrollment and broader enrollment criteria, allowing TiGenix to complete the study even faster. – Mark Curtis

FDA GRANTS SERVIER AND PFIZER IND CLEARANCE FOR UCART19

Servier, in collaboration with Pfizer has received an Investigational New Drug (IND) clearance from the FDA to expand the clinical development of their cellular therapy candidate, UCART19, in the USA, for the treatment of relapsed/refractory acute lymphoblastic leukemia.

UCART19 is a gene edited T-cell investigational drug that targets CD19, an antigen expressed on the surface of hematological malignancies. Unlike other CAR T therapy, UCART19 has the potential to overcome the limitation of the current autologous approach by providing an allogeneic, frozen, 'off-the-shelf' T-cell-based product.

Servier acquired exclusive rights to UCART19 from Cellectis in 2015. Later, Servier and Pfizer initiated a collaboration to develop this cancer immunotherapy. Under the terms of the agreement, Pfizer was granted exclusive rights by Servier to develop and commercialize UCART19 in the USA, while Servier retains exclusive rights for all other countries.

The IND clearance from the FDA means that Servier, with Pfizer's support, will be able to include several US centers in the ongoing CALM Phase 1 study on UCART19. The study was initiated in the UK and is an open label, dose-escalation study designed to evaluate safety, tolerability and anti-leukemic activity of UCART19 in patients.

As stated by Dr Patrick Thérasse, Director of Clinical Development Oncology at Servier, "we are very pleased that Servier's first IND approval has been granted for such an innovative approach as allogeneic CAR T therapy".

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AVROBIO EXPANDS PIPELINE TO TREAT GAUCHER DISEASE

The clinical stage biotechnology company Avrobio has expanded its rare disease gene therapy pipeline to treat Gaucher disease. The proof of concept for the therapy was demonstrated in Sweden, where the Gaucher disease program was also licensed. The therapy is the company's second targeting lysosomal storage disorders (LSDs) and will be part of a late-stage preclinical program.

Gaucher disease is caused by an inherited deficiency of the enzyme glucocerebrosidase and causes the build up of the fatty substance glucosylceramide in numerous tissues and organs. Avrobio's investigational treatment targets the faulty gene via a modification of the patient's own stem cells. A one-time treatment, it is delivered via infusion and expected to sustain a long-term supply of the endogenous enzyme. It is hoped that the treatment will be able to replace the current enzyme replacement course of treatment.

Geoff MacKay, Avrobio's President and CEO, has said: "Our talented team of industry veterans enables us to accelerate the development of this program with the ultimate goal of benefiting Gaucher disease patients worldwide. IND-enabling activities are currently underway in preparation for a Phase 1/2 clinical study. We are excited to add this program to our portfolio as we continue to focus on building our pipeline of gene therapies to treat rare diseases."

SANGAMO USES GENE REGULATION TECHNOLOGY TO LOWER TAU EXPRESSION

Sangamo Therapeutics has presented data demonstrating the efficacy of the company's zinc finger protein transcription factor (ZFP-TF)-mediated gene regulation technology. Results from the genome editing company show a significant reduction of tau mRNA and tau protein expression using human in vitro and animal models. Tau protein plays a pivotal role in various neurodegenerative diseases; Sangamo's data marks the first instance of a tau lowering agent demonstrating efficacy on neuritic dystrophy in an amyloid mouse model of Alzheimer's disease.

The studies from which the data has been procured were carried out in vitro using induced pluripotent stem cells (iPSCs) and mice cortical neurons, and in vivo using wild type mice and an amyloid mouse model. Single administrations of ZFP-TFs resulted in at least 80% reduction of tau mRNA and protein. Furthermore, specificity and off-target analysis in ZFP-TF-treated primary neurons revealed that tau was the only gene suppressed out of more

than 26,000 coding transcripts analyzed.

The mechanism of the ZFP-TF gene regulation technology represses or activates the expression of a specific endogenous gene or gene sequence to treat a broad portfolio of diseases. Other deployments of the technology include the down regulation of the mutant huntingtin allele that causes Huntington's disease. Sangamo intends to seek a partner with disease area expertise for the development and commercialization of its gene regulation approach for Alzheimer's and other tauopathies.

John B Penney Jr, Professor of Neurology, Harvard Medical School, has commented: "Of the many approaches to reduce tau expression that we've studied, zinc finger protein gene regulation technology is especially promising for its exquisite specificity, its potent reduction of tau protein expression, and its potential to provide a durable, long-lasting effect with only a single administration."

The competing hypotheses of beta-amyloid versus tau protein accumulation as the potential pathogenesis of Alzheimer's disease (AD) have been the focus of considerable research effort over the past two decades. The presentation of impressive preclinical data by Sangamo Therapeutics, using its ZFN technology, brings further support to the tau hypothesis. A reduction of >80% in tau mRNA and protein in the hippocampus of wild-type mice looks encouraging, given that an increase in tau deposits in the temporal lobe correlate with decreased performance in memory and attention in patients with early AD (Sci. Transl. Med. 2016; 8: 338). However, AD is becoming notorious for clinical trial failures for disease-modifying therapies, and recently published Phase 3 trial data on TauRx's methylthioninium-based tau reduction therapy provides little in the way of encouragement that targeting tau protein will lead to clinical success (Lancet 2016; 388: 2873–84). Sangamo certainly faces a long and rocky road ahead to develop this therapy – a case of high risk, but potentially high reward! – Richard Philipson

JUNO DISCONTINUES ITS LEAD CAR-T PROGRAM

Juno Therapeutics in collaboration with its partner Celgene, has made a strategic decision to discontinue its lead CAR-T trial (ROCKET) following patient deaths in 2016, which has hindered its odds of success. Juno now intends to switch its focus to JCAR017, a follow-up program that uses a defined CD4-CD8 composition that they think might improve the safety and efficacy in patients.

Juno's Phase 2 ROCKET trial was designed to evaluate the safety and efficacy of JCAR015 for the treatment of relapsed or refractory B-cell Acute Lymphoblastic Leukemia (B-ALL). JCAR015, the investigational product candidate, used genetically modified autologous T cells to eliminate leukemia cells. The infused T cells express a chimeric antigen receptor (CAR) that binds leukemia cells, which express the

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CD19 protein on the cell surface and initiate a cell-killing response against the cancer cell. Patients receiving CAR-T therapies received doses of chemotherapy beforehand to make the tumor more vulnerable to the CAR-T cells.

In July 2016, FDA had halted Juno's trial after three patient deaths. Juno had strongly suspected that these deaths occurred due to the chemotherapy agent fludarabine, despite its CAR-T rivals using the same drug did not cause patients to die. This clinical hold was later removed by FDA after Juno amended the protocol and decided to use cyclophosphamide as the pre-conditioning agent instead of fludarabine. They believed that this amendment would stop future deaths. However, two additional patient deaths later last year proved that fludarabine was not the only culprit.

Further investigation led to the identification of multiple factors that might have contributed to the increased risk in patients, including patient specific factors, the conditioning chemotherapy patients received, and factors related to the product. Hans Bishop, Juno's CEO, commented: "The delay with JCAR015 means it no longer makes sense to continue its development as we can instead bring forward a defined cell product candidate in a similar timeframe. We believe a defined cell product candidate, JCAR017, will have higher complete remission rates, a better tolerability profile and importantly get a greater percentage of patients into durable remissions."

JCAR017 uses a defined CD4:CD8 cell composition and 4-1BB as the costimulatory domain, which differentiates it from other CD19-directed CAR T product candidates in clinical development. Juno thinks this approach will reduce the variability of the composition of JCAR017 in what Juno sees as vital areas, such as the number of viable CD8 cells and the capacity to release inflammatory cytokines. It is currently being tested in a Phase 1 TRANSCEND trial designed to evaluate the safety and pharmacokinetics of this cell therapy in non-Hodgkin lymphoma patients.

NIGHTSTARX COMMENCES PHASE 1/2 TRIAL FOR RETINITIS PIGMENTOSA

The world's first clinical trial to treat the currently untreatable, orphan disease X-Linked Retinitis Pigmentosa (XLRP), a common cause of blindness in young people, has commenced. The Phase 1/2 trial is being carried out by NightstaRx Ltd, a company that develops gene therapies for inherited retinal dystrophies. In 18 months, the viral vector has progressed from licensing to the trialling. The treatment employs an adeno associated virus (AAV) to deliver a codon optimized copy of the retinitis pigmentosa GTPase regulator RPGR gene into cells of the eye.

The multicenter trial will be carried out in the UK with patients enrolled at Opthamology centres of excellence, such as Oxford and Manchester. The primary endpoint

of the study is to assess the safety and tolerability of receiving a single, subretinal injection of AAV-XLRP-GR over a 12-month period. The cohort will comprise at least 24 male patients in an open-label, dose escalation design.

Robert MacLaren, Professor of Ophthalmology at the University of Oxford and principal investigator, commented: "X-linked retinitis pigmentosa is a devastating disease of early onset that leads to blindness in males. Many individuals are legally blind in their teens, and there is currently no treatment available. Based on previous findings in preclinical in vivo disease models, which have shown significant rescue of photoreceptors, we believe this approach has great potential to restore or maintain sight in patients. The unique codon-optimisation strategy overcomes the inherent instability problems of RPGR that confounded earlier attempts at gene replacement."

The race to develop a gene therapy treatment for X-linked retinitis pigmentosa (RP) continues apace. An estimated 10 to 20% of cases of RP are X-linked, and more than 70% of X-linked cases are caused by mutations in the RP GTPase regulator RPGR gene, leading to estimates that more than 20,000 people in the USA and the European Union could potentially benefit from a gene therapy-based product. NightstaRx has started a Phase 1/2 trial using its AAV vector to deliver a codon-optimised copy of RPGR administered as a sub-retinal injection. This appears to put it ahead of competitors MeiraGTx and AGTC, both of which are also developing AAV vectors to deliver RPGR, but which remain at the preclinical stage of development. It remains to be seen whether NightstaRx's codon-optimised technology will keep it ahead of its competitors, and it will be interesting to see which company eventually wins the race to market! – Richard Philipson

FDA CLEARANCE FOR FATE'S NK CELL THERAPY

Fate Therapeutics, a US-based clinical-stage biopharmaceutical company, has been granted IND clearance from the FDA for FATE-NK100, an adaptive memory natural killer (NK) cell product candidate. FATE-NK100 is being developed to target advanced acute myeloid leukemia (AML). The IND approval will see a first-in-human clinical trial and is expected to enrol AML patients at the Masonic Cancer Center, University of Minnesota following approval of the Center's institutional review board.

AML patients have poor prognosis and few therapy options if they relapse or refract from front-line treatments. FATE –NK100 is comprised of adaptive memory NK cells, has demonstrated enhanced anti-tumor activity, increased persistence, and resistance to immune checkpoint pathways in preclinical studies when compared with current NK cell therapies. When

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administered with a monoclonal antibody, it has also been shown to augment antibody-directed cellular cytotoxicity against cancer cells.

Fate Therapeutic's first-in-human study is designed to evaluate the safety and determine the maximum dose of a single intravenous infusion of FATE-NK100 in subjects with refractory or relapsed AML. Secondarily, the investigation will assess the anti-tumor activity, including rates of complete response, clearance of minimal residual disease, disease-free survival and overall survival. The trial will employ accelerated dose escalation, which will test up to four doses of FATE-NK100 with one subject enrolled per dose level until a dose-limiting toxicity (DLT) is observed. In the event of a DLT observation, the study will convert to a 3+3 design and enroll a ten subject expansion cohort at the maximum dose level.

Scott Wolchko, President and CEO of Fate Therapeutics, commented: "FATE-NK100 is a first-in-class NK cell product candidate designed to enhance direct tumor cell killing, resist immune checkpoints and promote endogenous T-cell anti-tumor response. We look forward to exploiting the multifaceted effector function of these adaptive memory NK cells across liquid and solid tumors, both as a monotherapy and in combination with therapeutic antibodies."

KITE SUBMITS BLA FOR ITS CAR-T THERAPY TO TREAT NHL

Kite Pharma has submitted a Biologics License Application (BLA) to the FDA for its lead product candidate, axicabtagene ciloleucel (previously known as KTE-C19). The submission was completed on a rolling basis for the first CAR-T therapy which is intended to treat patients with relapsed or refractory aggressive non-Hodgkin lymphoma (NHL) who are ineligible for autologous stem cell transplant (ASCT).

Previously, the FDA granted axicabtagene ciloleucel Breakthrough Therapy Designation (BTD) for diffuse large B-cell lymphoma (DLBCL), transformed follicular lymphoma (TFL), and primary mediastinal B-cell lymphoma (PMBCL). The BLA submission followed positive results from axicabtagene ciloleucel's ZUMA-1 pivotal trial. The trial was supported by funding from the Leukemia & Lymphoma Society's (LLS) Therapy Acceleration Program® (TAP).

Kite currently holds Priority Medicines (PRIME) regulatory support for DLBCL in the EU, and is planning a regulatory submission to the European Medicines Agency (EMA) for axicabtagene ciloleucel this year. Approval of the BLA will instigate the commercial launch axicabtagene ciloleucel in the company's home country, the USA.

Axicabtagene ciloleucel is an investigational therapy in which a patient's T cells are engineered to express a chimeric antigen receptor (CAR) to target the antigen CD19, a protein expressed on the cell surface of B-cell lymphomas and leukemias, and redirect the T cells to kill cancer cells.

DATA PUBLISHED ON FIRST SCD PATIENT TREATED WITH GENE THERAPY

Data from Patient 1204, a 13 year old with severe sickle cell disease (SCD) who received bluebird bio's gene therapy product, Lentiglobin, has been published in the *New England Journal of Medicine*.

The treatment was part of the HGB-205 clinical study and involves receiving an autologous stem cell transplant. Data published reflected 15 months of follow up from the treatment. An additional 6 months of follow up has been presented at the *58th American Society of Hematology* Annual Meeting in December 2015. Thus far the patient has been free from severe symptoms and has resumed normal activities as a result of the LentiGlobin treatment.

The study was carried out at the Necker Hospital, Assistance Publique-Hopitaux de Paris where Patient 1204's SCD had been managed for 10 years prior to the study. The LentiGlobin therapy was able to eliminate the need for blood transfusions, which the patient had previously been requiring on a monthly basis. The therapeutic approach was initially trialled in mouse models, the results of which were published in 2001.

For the autologous stem cell transplant, hematopoietic stem cells (HSCs) were collected from two bone marrow harvests. From the bone marrow, $CD34^+$ cells were enriched and transduced with BB305 lentiviral vector. Patient 1204 was subject to daily pharmacokinetic studies and dose adjustment for the duration of treatment, and 88 days after transplantation, blood transfusions were able to be discontinued.

MEDIGENE TO INITIATE A TCR CANCER IMMUNOTHERAPY PHASE 1 TRIAL

Medigene, a biotechnology company headquartered in Munich, has announced details on the company's first clinical trial with T-cell receptor-modified T cells. Subject to regulatory approval, Medigene intends to use an HLA-A2:01-restricted T-cell receptor (TCR) that targets a well-characterized tumor antigen, preferentially expressed antigen in melanoma (PRAME), in a combined Phase 1/2 safety and feasibility trial. The trial intends to enrol patients with advanced hematological diseases, namely acute myeloid leukemia (AML), myelodysplastic syndrome (MDS) and multiple myeloma (MM).

At present, Medigene uses PRAME as a target in its ongoing DC-vaccine trial in AML, where the favorable safety profile of this vaccine allowed the trial to advance into Phase 2. PRAME has been shown to be overexpressed in various solid cancers and hematological malignancies, while its expression is mainly limited to testis in normal

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circumstances. For this reason, it's an ideal candidate for adoptive TCR therapy. The TCR technology aims to equip the patient's own T cells with tumor-specific T-cell receptors. The receptor-modified T cells are then able to detect and efficiently kill tumor cells.

Medigene has established Good Manufacturing Practice (GMP)-compliant processes for their combination with patient-derived T cells, in preparation for their anticipated first-in-human TCR trial. The Phase 1 trial (MDG1011) is designed as a dose escalation study in which up to four dose cohorts will be tested in a 3+3 design. The company plans to further test the chosen dose in a Phase 2 trial and might potentially extend the study to other malignancies as well.

Professor Dolores Schendel, CEO and CSO of Medigene, commented: "Based on extensive preclinical assessment, we are convinced that our TCR specific for the PRAME antigen with high avidity, potent antitumor efficacy and a favorable safety profile will enable us to execute a unique clinical program. This particular trial design examining various indications in parallel allows for faster decisions about future clinical development options based on multiple clinical data sets."

Medigene announced the selection of its first TCR target, joining a small group of companies, including Adaptimmune/GSK and Bellicum, targeting preferentially expressed antigen in melanoma (PRAME). Medigene will initially enter the (crowded) hematological malignancy space but believes it will be able to target solid tumour indications as well. PRAME makes a nice target for adoptive cell therapy as its expression is isolated to the testis, and almost non-existent elsewhere in the body. – Mark Curtis

HITACHI TO PURCHASE PCT FROM CALADRIUS BIOSCIENCES

Caladrius Biosciences has announced that it has signed a definitive agreement with Hitachi Chemical Co. America, Ltd (Hitachi), in which its remaining 80.1% interest in its subsidiary, PCT, will be purchased by Hitachi. PCT, a well-known development and manufacturing services provider exclusively focused on the cell therapy industry, is currently 19.9% owned by Hitachi. The remaining interest will be purchased for $75 million in cash; and in addition there is the potential for Caladrius to receive an additional cash payment of $5 million if PCT achieve certain revenue-based milestones.

This transaction will redefine Caladrius as a cell therapeutics-only development company with multiple proprietary technology

platforms. The proceeds from the purchase is earmarked for working capital. This will fund projects including Caladrius' currently enrolling Phase 2 trial for its lead product candidate, CLBS03 for the treatment of recent-onset Type 1 diabetes. The transaction will also allow for the judicial and opportunistic identification of clinical development pipeline candidates and the elimination of the company's remaining $5.5 million of outstanding debt.

A $5 million payment from Hitachi to Caladrius was triggered upon signing the agreement and $70 million is due upon closing, which is subject to approval by Caladrius' shareholders and customary closing conditions. The agreement also provides for Hitachi /PCT to continue to provide development services to Caladrius' T regulatory cell program, for a period of seven years after closing.

Dr David J Mazzo, CEO of Caladrius, commented: "Hitachi Chemical's purchase of our remaining interest in PCT unlocks the value of this asset for our Company both by transforming Caladrius into a well-capitalized pure play therapeutics development company and by eliminating our need to contribute the tens of millions of dollars of future capital investment in PCT needed for it to fully realize its cell therapy commercial manufacturing growth goals." Hitachi, by contrast, has the capacity to deploy the capital and access to engineering expertise required by PCT.

THERMO FISHER SCIENTIFIC AND CGT CATAPULT COLLABORATE TO OPTIMIZE SUPPLY CHAIN

To provide developers with a seamless supply chain for gene therapy development and commercialization, Thermo Fisher Scientific and Cell and Gene Therapy Catapult (CGT Catapult) have announced a collaboration. The partnership will address challenges surrounding manufacturing capability, distribution, logistics and storage capacity with the hope of accelerating the development of cell and gene therapies.

A key part of the collaboration involves locating Fisher Bioservices' CryoHub in CTG Catapult's new large-scale cell and gene therapy manufacturing centre in Stevenage, UK. The CryoHub will be able to support the delivery of cells to clinical studies and early commercial supply through a cryogenic storage, distribution and logistics solution. Operating on a modular model, the hub will be able to flexibly accommodate the needs of both early stage and large-scale operations. The proximity of the hub to CTG's manufacturing centre will aid the conduction of clinical trials and access to therapies by streamlining the geographies of the supply chain.

The collaboration is supported by the UK government, with the anticipation of enhancing the attractiveness of the UK as a location for companies to develop, manufacture and export from.

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USPTO REJECTS FOURTH RE-EXAMINATION REQUEST AGAINST CELYAD'S US PATENT

The US Patent and Trademark Office (USPTO) has rejected a new re-examination request of Celyad's allogeneic TCR-Deficient CAR-T Cells (US Patent No. 9,181,527). The patent, owned by the US and Belgium-based company, relates to allogeneic human primary T cells that are engineered to be TCR-deficient and express a CAR and remains valid and enforceable.

The patent has now been challenged on four occasions, each time with an outcome that is favorable to Celyad, a clinical-stage biopharmaceutical company specialized in the discovery and development of engineered cell-based therapies.

"This patent is key for the players that are developing in the USA allogeneic CAR-T cell approaches and it places Celyad in a very good position to optimize the significant potential of its allogeneic platform, either on our own or through strategic collaborations," said Christian Homsy, CEO of Celyad.

Celyad is currently employing the patent with its Natural Killer Receptor based T-Cell (NKR-T) platform that has the potential to treat a broad range of solid and hematologic tumors. It is being investigated in THINK (THerapeutic Immunotherapy with NKR-2) trial, a multinational (EU/US) open-label Phase 1 study to assess the safety and clinical activity of multiple administrations of autologous CAR-T NKR-2 cells in seven refractory cancers. In contrast to traditional CAR-T therapeutic approaches, and based on strong preclinical evidence, Celyad's CAR-T NKR-2 program does not use patient lymphodepleting pre-conditioning, hence avoiding the toxicities associated with chemotherapy and allowing the immune system to remain intact.

CELL MEDICA RAISES £60 MILLION IN SERIES C FINANCING

Cell Medica, a London-based pharmaceutical company specialized in the development of cellular therapeutics for the treatment of cancer and infectious diseases, has announced that it raised £60 million in a Series C financing.

Cell Medica will use the funds to advance development of its three proprietary technology platforms for cell-based immunotherapy products and to expand its portfolio in immune-oncology. Touchstone Innovations participated in the Series C alongside Neil Woodford's funds and Invesco Perpetual. These were the three organizations which drove Cell Medica to a £50 million Series B round late in 2014.

The Company's lead product, baltaleucel-T (CMD-003), is currently under investigation in the

CITADEL Phase 2 clinical trial for the treatment of patients with advanced lymphomas associated with the Epstein–Barr virus. baltaleucel-T is comprised of the patient's own immune cells and is expected to offer the potential for a targeted approach to cancer treatment with very limited side effects or toxicities. In February 2017, the US FDA granted fast track designation to baltaleucel-T for the product's potential to address an important unmet clinical need.

As part of the company's effort to expand its portfolio, the company had signed a co-development partnership with Baylor College of Medicine in 2016 to develop engineered immune cell-based technologies for the treatment of solid tumors. The collaboration aimed to apply CAR technology to Natual Killer T cells as a novel immune cell type with biological properties that may be particularly effective for targeting solid tumors. In June 2016, Cell Medica acquired Swiss-based Delenex Therapeutics to advance next-generation CAR-modified cellular immunotherapies with improved functionality and specificity.

Gregg Sando, CEO of Cell Medica, commented: "With the strong support of our key shareholders, Cell Medica will implement the next phase of our development programme, bringing a new generation of cell-based immunotherapy products into Phase 1 clinical trials as well as completing our Phase 2 program for baltaleucel-T."

New executives appointed by bluebird bio

Cell Medica was successful in raising $60 million to continue advancing its autologous T-cell platform. The company's technology is unique in that it is designed to expand T cells against specific viral targets, including EBV and HPV. The company previously expanded its pipeline through a deal with Baylor and a takeover of Switzerland-based Delenex, an antibody therapeutics company. The deal with Baylor is focused on delivered off-the-shelf (donor-derived) cell-based immunotherapies, while the Delenex deal give Cell Medica the expertise and IP necessary to create proprietary CAR products. With this money in hand the company can begin to build what should be a diverse and interesting portfolio of products. – Mark Curtis

SOLID BIOSCIENCES RAISES $50 MILLION IN SERIES C FINANCING

Solid Biosciences, a company with a portfolio targeting Duchenne muscular dystrophy (DMD), has completed its initial closing of Series C financing worth $50 million. The round was led by RA Capital Management and Bain Capital Life Sciences alongside

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funds from existing investors Perceptive Advisors, Janus Capital Management and Biogen. A number of new companies also contributed to the round.

The financing will be primarily focused on advancing the investigational gene therapy, SGT-001, into the clinic in the second half of 2017. In the long-term, the company also aims to secure manufacturing capabilities and support for the clinical and commercial needs of its DMD programs.

The transaction also involved a merge with Solid GT, a subsidiary focused on gene therapy development. This move will see a consolidation of the two Boards of Directors in an effort to align talent and resources most effectively.

CEO Ilan Ganot commented: 'The proceeds will enable us to move SGT-001 through clinical development and maintain momentum in our efforts to identify and develop a new generation of meaningful DMD therapies".

ADIPOSE STEM CELL THERAPY BAGS $20 MILLION IN SERIES D FINANCING

Sanford Health, an integrated health system provider has invested $20 million in InGeneron's adipose stem cell therapy to treat various orthopedic conditions.

InGeneron is a Houston, Texas-based regenerative medicine and cell therapy company focused in developing adipose stem cell therapy to treat various orthopaedic and wound healing indications. The company uses its proprietary technology, which enables physicians to use adipose-derived regenerative cells from the patient's own body for immediate therapeutic application at point of care.

The current Series D funding is in addition to the existing collaboration between InGeneron and Sanford Health to conduct clinical trials to treat rotator cuff tears and venous ulcers at different sites in the Sanford Health network. The studies aim to investigate the safety and efficacy of using autologous adipose-derived regenerative cells in patients compared to current standard of care treatments. With the aim of regulatory approval in the USA, the first patients were enroled in InGeneron's clinical program in January 2017.

The trial uses stromal vascular fraction, a mixture of cells and nutrients isolated from a patient's own body that contain adipose-derived stem cells, as a potential therapy for partial-thickness rotator cuff tears. Sanford scientists and clinicians are exploring the application of this type of stem cells for other conditions.

Ron Stubbers, President of InGeneron, commented: "This significant investment demonstrates Sanford's commitment to be an active participant in InGeneron as well as being our clinical trial site of choice. Our joint efforts will enable the company to make regenerative cell therapies available to clinical practice and to establish a leading position in the application of adipose-derived regenerative cells."

NEW EXECUTIVES APPOINTED BY BLUEBIRD BIO

bluebird bio, a clinical stage gene therapy company has appointed a new Chief Technology and Manufacturing Officer, Derek Adams, and a new Senior Vice President, Corporate Development and Strategy, Joanne Smith-Farrell. The appointments come at a time when the company is preparing for upcoming regulatory filings and commercial launches.

Dr Adams joins bluebird from Evelo Biosciences where he was the Senior VP of CMC. Previously he was VP of Technical and Strategic Product Development at Alexion Pharmaceuticals. The experience that he brings to bluebird includes establishing process development and supply chains for clinical studies and global manufacturing processes support and development.

Dr Smith-Farrell previously served as VP, Business Development Transactions at Merck, Inc. and was VP of Strategic Transactions at Pfizer. A Fellow in Biomedical and Chemical Engineering at the Harvard-MIT Division for Health Science and Technology, she has received the NIH National Service Award in Research.

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