

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: This month illustrates the mixed fortunes of companies working in cell and gene therapy. Whilst Spark Therapeutics continues to roll out positive clinical data in the rare eye disease Leber's congenital amaurosis-2, and Agilis Biotherapeutics announced authorization of a Phase IIb trial in the rare CNS disease aromatic-L-amino acid decarboxylase deficiency, there is less good news from Adverum, which announced a 1-year delay to its alpha-1-antitrypsin deficiency program due to manufacturing issues. Adverum uses a baculovirus-based AAV production system; whilst these systems are scalable, they can present problems with low yields and baculovirus stability. R&D in gene therapy is as healthy as ever, but manufacturing can often prove to be the Achilles heel for the field.



GENE THERAPY
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CELL THERAPY: Organova has been busy working for some time now on developing 3D bio-printed tissues for use in screening drug candidates. The theory being that Pharma can save dollars by adopting screens that provide greater 'predictiveness'. It's a tough business model. Cellular Dynamics International, now owned by FujiFilm,

burnt through a great deal of money in its day trying to persuade Pharma to screen compounds with its cell lines. Organovo upped the ante, though, with its printing platform, creating 3D, multi-cellular aggregates, or 'organoids', which more closely resemble real tissue. The company announced a collaboration with Merck in 2015, giving Merck access to its human liver tissue platform for drug development. Now, Organovo has plans to transcend tools into the realm of therapeutics, and will bring its bio-printed tissue into the clinic, initially for liver disease. Ambitious? Absolutely, but it's a small step towards realizing the big vision of artificial organ replacement.



ADVERUM DELAYS GENE THERAPY TRIAL FOR ALPHA-1 ANTITRYPSIN DEFICIENCY

Adverum Biotechnologies, a California-based gene therapy company focusing on the discovery and development of therapeutics for retinal and rare diseases, has delayed the initiation of its Phase I/II gene therapy trial for the treatment of alpha-1 antitrypsin (A1AT) deficiency by 12 months.

Adverum, formerly known as Avalanche Biotechnologies, has explained that this delay in its ADVM-043 trial is due to its need to upgrade the manufacturing process and transfer it to a third-party contract manufacturer. Through this, the company aims to increase the production scale so that the same manufacturing process is used from clinical trials through to the commercial stage. Adverum expects to begin enrolment of patients in the fourth quarter of 2017.

The ADVM-043 trial is designed to deliver *A1AT* gene in patients with A1AT deficiency, a rare genetic disorder that results in serious respiratory and liver disease. The trial uses Adverum's industrialized manufacturing process based on its baculovirus expression system and

the company claims this next generation expression system as highly efficient and scalable, with production yielding up to 100-times greater than those obtained using conventional adeno-associated virus (AAV)-based production systems.

The company's other lead programs for wet age-related macular degeneration and hereditary angioedema are not affected and it is in preparation to initiate toxicology studies in the first half of 2017.

Dr Amber Salzman, Adverum's new CEO, commented: "Adverum has industry-leading capabilities in process development and manufacturing, consisting of a baculovirus-based AAV production system and state-of the-art purification technology to manufacture AAV vectors of various serotypes. This allows us to deliver a turn-key large-scale process to third-party cGMP manufacturers. We plan to leverage our leading manufacturing capabilities and upgrade our ADVM-043 manufacturing process now, to prepare for both our anticipated clinical and commercial product needs."



BONE'S CELL THERAPY SHOWS POSITIVE EFFICACY OUTCOME FOR DEGENERATIVE SPINE DISORDERS

Bone Therapeutics, a Belgium-based pharmaceutical company specialized in the development of cell therapy products for bone fracture repair, has announced positive efficacy data for its Phase IIa spinal fusion trial with allogeneic osteoblastic cells (ALLOB®).

The current Phase IIa trial is designed as a pilot, multicenter, open-label study to evaluate the safety and efficacy of ALLOB® implantation to the standard of care procedure in lumbar spinal fusion for degenerative disc diseases. Results obtained from the first half of patients indicate significant clinical improvements in pain, function and general health of the patients as early as 6 months. More interestingly, all patients who received the treatment have met the primary and secondary endpoints at the end of the 12-month follow-up period.

The procedure involved a single administration of ALLOB and ceramic scaffold mix into the lumbar interbody fusion site. Primary endpoints of the study included radiological evaluation of fusion, improvement in pain and functional disability and safety.

Spine fusion was assessed using radiological and clinical evaluation.

In this group of 8 patients, CT scans showed the presence of bone bridges from 6 months in 75% of assessable patients. Back and leg pain improved by 50 and 80%, respectively, and the general health status improved by 50% after 6 months.

ALLOB is currently being evaluated in three Phase I/IIa clinical trials for delayed-union fractures, spinal fusion and the revision of failed spinal fusions. ALLOB has been classified as a tissue engineered product under the ATMP regulation and received orphan drug designation from the European Medicine's Agency (EMA) and US Food and Drug Administration (FDA) for two indications: osteonecrosis and osteogenesis imperfecta.

Enrico Bastianelli, CEO of Bone Therapeutics commented: "Seeing evidence of fusion and the clinical improvements in these patients as early as 6 months strengthens our confidence in the potential of ALLOB to become an important addition to the current standard of care. These results give us great confidence for the remainder of the trial for which we expect the full set of data in Q2 2017."



TFDA APPROVES PHASE IIB GENE THERAPY TRIAL FOR AADC DEFICIENCY

Agilis Biotherapeutics, a US-based biotechnology company specialized in the development of gene

therapies for rare genetic diseases of the central nervous system, has announced that the Taiwan Food and

Drug Administration and the ethics committee at National Taiwan University have authorized its Phase IIb clinical trial for the treatment of Aromatic L-Amino Acid Decarboxylase (AADC) deficiency.

AADC deficiency is a rare genetic condition arising from a deficiency in AADC, which catalyzes the final step in the synthesis of the neurotransmitters, dopamine and serotonin. AADC deficiency is caused by mutations in the dopa decarboxylase gene.

The trial, AGIL-AADC, will be performed under the direction of Professor Paul Hwu at NTU Hospital. AGIL-AADC is an adeno-associated virus vector containing the human gene for the AADC enzyme. Dr Hwu and colleagues have treated 18 subjects to date in two prospective clinical studies using a single administration of the gene therapy. The present Phase IIb study

will enroll a third cohort of patients into two parts, one evaluating the AGIL-AADC gene therapy dose used in prior studies and a second exploring single administration of an increased dose.

Dr Christopher Silber, CMO of Agilis, commented: "Clinical development of AGIL-AADC continues to be very encouraging, with long-term follow-up and data collection for treated patients providing an opportunity for ongoing assessment of the durability of functional improvements and safety profile. Advancing our understanding of dose range will be informative as we continue to strive to position AGIL-AADC for registration. Given the devastating clinical course of AADC deficiency and refractoriness to standard therapies, our mission for these patients is to provide a novel intervention to improve their condition and enhance their lives."



KITE PHARMA INITIATES ZUMA-6 TRIAL IN PATIENTS WITH REFRACTORY DIFFUSE LARGE B-CELL LYMPHOMA

Kite Pharma, the California-based biopharmaceutical company, has initiated a Phase 1/2 combinatory clinical trial in patients with refractory diffuse large B-cell lymphoma (DLBCL). The study has enrolled its first patient and will evaluate the safety and efficacy of Kite's lead product candidate, KTE-C19 in combination with atezolizumab, Genentech's anti-PD-L1 cancer immunotherapy.

KTE-C19 is 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. Based on the preliminary evidences obtained, Kite hopes that the use of two compounds in combination will provide a synergistic effect.

The ZUMA-6 trial, which is a collaboration between Kite and Genentech, is designed as a single-arm, open-label, multicenter study in patients with chemotherapy-refractory DLBCL. The treatment procedure includes administration of a conditioning chemotherapy regimen of fludarabine and cyclophosphamide followed by a single

infusion of CAR transduced autologous T cells administered intravenously followed by a limited course of atezolizumab.

The Phase I part of ZUMA-6 will evaluate the safety of KTE-C19 and atezolizumab given in sequence. The primary objective of the Phase II portion is to evaluate the combination's safety and efficacy. The study is expected to complete by 2023.

Dr David Chang, Kite's CMO, commented: "The ZUMA-6 combination study is a core element of our broad strategy to optimize KTE-C19 treatment outcomes and to significantly extend the important potential benefits of KTE-C19 monotherapy. We view the scientific rationale for this combination study as compelling and look forward to advancing the study based on our extensive clinical experience."



AVEXIS PRESENTS UPDATE ON ITS GENE THERAPY TRIAL FOR SPINAL MUSCULAR ATROPHY

AveXis, a clinical-stage gene therapy company specialized in the development of treatments for orphan and life-threatening neurological diseases, has presented interim data of its Phase I gene therapy trial for the treatment of spinal muscular atrophy (SMA).

AVXS-101 is a gene therapy candidate developed for the one-time treatment of SMA type 1 and is the only gene therapy in development for SMA. The data presented by Dr Jerry Mendell of Nationwide Children's Hospital, at the *21st International Annual Congress of the World Muscle Society* in Spain revealed the favorable safety profile of AVXS-101 and showed that the treatment was generally well tolerated by the subjects, with no new treatment-related concerns identified.

SMA is a severe neuromuscular disease characterized by the loss of motor neurons leading to progressive muscle weakness and paralysis. It results from a genetic defect in the SMN1 gene, which codes for the survival motor neuron (SMN) protein, and affects all muscles in

the body. There is no effective treatment for SMA and current drug therapy has been unsuccessful in stabilizing or reversing this disease. SMA Type 1 is one of the leading genetic cause of infant mortality.

Interim data of the second cohort of patients who received the proposed therapeutic dose of gene therapy showed that the patients achieved key motor development milestones as of mid-September 2016. Of the total 12 patients in this cohort, 8 have achieved the ability to sit unassisted, 11 achieved head control, 7 have acquired the ability to roll over completely and 11 could sit with support. Two patients who had achieved earlier and important developmental milestones such as crawling, standing with support, standing alone and walking with support have now started walking independently.

The trial is designed as an open-label, dose escalation study to determine the safety and efficacy of gene transfer in SMA type 1 patients. The procedure involves intravenous injection of AVXS-101

through a peripheral limb vein and short-term safety will be evaluated over a period of 2 years. Patients will be tested at baseline and return for follow-up visits on days 7, 14, 21 and 30, followed by once every month through 12 months' post-dose, and then every 3 months through 2 years post-infusion. The trial is expected to complete in December 2017.

Sean P Nolan, president and CEO of AveXis, commented: "To date, the

majority of patients who received the proposed therapeutic dose of AVXS-101 have achieved key milestones and two-thirds of these patients can sit independently – a fact completely inconsistent with the known disease course, as children with untreated SMA Type 1 will never sit unassisted. We are encouraged by these interim data, and continue to work diligently to bring this gene therapy to the children suffering from this devastating condition."



ADAPTIMMUNE AMENDS THE PROTOCOL OF ITS T-CELL THERAPY FOR OVARIAN CANCER

Adaptimmune Therapeutics, a clinical-stage company focusing on the development of cancer immunotherapy products based on its Specific Peptide Enhanced Affinity Receptor (SPEAR™) T-cell platform, has amended the protocol of its T-cell therapy trial for the treatment of refractory metastatic ovarian cancer. Through the addition of fludarabine to the preconditioning regimen, the company hopes to induce objective clinical responses in ovarian cancer patients.

The news has, however, had a negative effect on Adaptimmune with shares dropping by 12% as investors have lost confidence in the trial due to its lack of efficacy and the latest addition of fludarabine, which was linked to patient deaths in Juno's CAR-T trial.

The current Phase I/IIa trial is an open-label, multicenter study to assess the safety and tolerability of Adaptimmune's autologous engineered T cells in patients with treatment-resistant or refractory metastatic ovarian cancer expressing

the NY-ESO-1 antigen. The initial patients had received a preconditioning regimen of cyclophosphamide alone and no objective clinical responses were observed in any of the patients. Data from its NY-ESO SPEAR T-cell therapy in synovial sarcoma patients indicated the importance of including fludarabine in the preconditioning regimen and therefore the company has decided to use fludarabine in this trial as well, for the treatment of ovarian cancer. The trial will enroll up to 10 patients under the revised protocol including a preconditioning regimen that includes fludarabine in combination with cyclophosphamide.

Dr Rafael Amado, Adaptimmune's CMO, commented: "Based on our clinical experience to date, we have amended the protocol for this trial to include both fludarabine and cyclophosphamide in the conditioning regimen. We hope that, as previously observed in synovial sarcoma, this lymphodepleting regimen will enable anti-tumor immune responses mediated by NY-ESO SPEAR

T-cell therapy in these patients with advanced chemotherapy relapsed or refractory ovarian cancer.”

In additional news this month, Adaptimmune has initiated a Phase I triple tumor study in patients with inoperable or metastatic urothelial cancer, melanoma or squamous cell carcinoma of the head and neck.

The study is designed as an open-label, multicenter, dose escalation study to assess the safety and tolerability of SPEAR® T-cell therapy targeting the MAGE-A10 antigen in patients with inoperable or metastatic urothelial cancer (transitional cell cancer of the bladder, ureter or renal pelvis), melanoma

or squamous cell carcinoma of the head and neck. Up to 12 patients are expected to be included in this Phase I trial, with the first patient enrolled at the MD Anderson Cancer Center.

The company will conduct the trial in collaboration with the University of Texas MD Anderson Cancer Center. Both the parties had entered a strategic agreement to expedite the development of adoptive T-cell therapies for multiple types of cancer and are collaborating in several preclinical and clinical development of Adaptimmune’s first- and second-generation SPEAR T-cell therapies.



OPEXA'S T-CELL THERAPY FAILS TO MEET EFFICACY ENDPOINTS

Opexa Therapeutics, a Texas-based biopharmaceutical company specialized in the development of personalized immunotherapies for autoimmune disorders, has announced that its Phase IIb Abili-T trial of Tcelna® has not met the primary and secondary endpoints in patients with secondary progressive multiple sclerosis (SPMS).

Tcelna consisted of an autologous pool of myelin reactive T cells expanded *ex vivo* with immunodominant epitopes selected from three myelin antigens. The cells were attenuated by irradiation to prevent further proliferation before releasing product for administration. Approximately 5 weeks after receipt of the subject’s whole blood, the subjects received either Tcelna (30–45 x 10⁶ cells in 2 ml) or placebo (Tcelna excipients) and received two annual courses of five subcutaneous doses each year (at 0, 4, 8, 12 and 24 weeks).

The Abili-T clinical trial was designed as a randomized, double-blind, placebo-controlled study to evaluate the safety and efficacy of Tcelna in SPMS patients. The study included 183 patients and was conducted at 35 clinical trial sites in the USA and Canada. The endpoints of the study included a reduction in brain volume change (primary) and a reduction in the rate of sustained disease progression (secondary). Although Tcelna showed a favorable safety and tolerability profile, it did not meet both the primary and secondary endpoints.

Neil K Warma, President and CEO of Opexa, commented: “We are disappointed that Tcelna did not meet the predefined endpoints in the Abili-T trial. We will evaluate the full data set over the coming weeks and review cash preservation options while we consider the best path forward for the company.”

EXPERT
PICKOPEXA THERAPEUTICS MISSED PHASE IIB
ENDPOINT

Underscoring the challenges in developing novel therapies for multiple sclerosis, Opexa Therapeutics announced its T-cell immunotherapy for secondary progressive MS did not meet its primary or secondary endpoints. Opexa's approach is to isolate and expand myelin reactive T cells from a patient, and re-introduce these T cells in an attempt to stimulate an immune response against T-cell subsets that are at the root of myelin destruction. The therapy was developed to be administered several times, and to be unique to a patient's epitope profile as it evolves over time. An eloquent approach, but the company will have to go back to the drawing boards to determine a future clinical strategy. – Mark Curtis

CEDARS-SINAI RECEIVES FDA
APPROVAL TO EVALUATE STEM CELL
GENE THERAPY IN ALS PATIENTS

The FDA has granted approval to Cedars-Sinai investigators to test a combination of stem cell-gene therapy for the treatment of amyotrophic lateral sclerosis (ALS).

ALS is a progressive adult-onset neurodegenerative disease that primarily affects upper and lower motor neurons, but also frontotemporal and other regions of the brain. ALS leads to paralysis and death within 5 years after its onset. To date, there is no effective treatment for the disease and therapeutic trials in animal models have not been able to predict significant treatment response in humans.

The current stem cell-based gene therapy trial is designed to assess the safety and tolerability of the combination of stem cell and gene therapy approach to preserve leg mobility in patients with ALS. The trial, which is expected to begin by the end of 2016, will be led by Dr Robert Baloh and Dr Peggy Allred. The 18 ALS patients will receive the investigational

treatment at the Cedar-Sinai Board of Governors Regenerative Medicine Institute.

The research that led to the development of this approach was funded by the California Institute for Regenerative Medicine and it involves genetically engineering stem cells to produce a protein, glial cell line-derived neurotrophic factor (GDNF). Prior studies have shown that the stem cells producing GDNF holds the ability to protect motor neurons and transmit impulses from the brain or spinal cord to the muscle. These engineered stem cells are replicated until billions of cells are formed *in vitro* and are infused into the patient's spinal cord. Stem cells differentiate into glial support cells that produce GDNF and are hoping to keep the motor neurons alive.

Dr Clive Svendsen, director of the Cedars-Sinai Board of Governors Regenerative Medicine Institute, commented: "Motor neurons

that die in ALS don't exist in a vacuum – they have support cells called glia that enable the motor neurons to live and operate. What we and others have found in ALS is that the support cells become sick and lack

certain proteins that keep motor neurons alive. When the support cells die, the motor neurons also die, causing paralysis that gets worse and worse until the patient can no longer move.”



SOLID'S GENE THERAPY CANDIDATE RECEIVES ORPHAN DRUG DESIGNATION

Solid Biosciences, a life sciences company focusing on the development of therapies for Duchenne muscular dystrophy (DMD) has received orphan drug designation from the FDA and European Commission for their gene therapy candidate SGT-001, developed for the treatment of DMD.

SGT-001 is an adeno-associated viral (AAV) vector-mediated gene therapy that has the potential to express micro-dystrophin, a shorter form of the dystrophin protein that is lacking in patients with DMD. Preclinical studies have shown that single administration of SGT-001 resulted in long-term expression of micro-dystrophin in muscle.

Solid has opened an office in London to support the advancement of

its clinical program. UCL's Dr Valeria Ricotti and patient advocate Kerry Rosenfeld will work closely with the European DMD community to advance this therapy in DMD patients. The company plans to initiate the clinical studies for SGT-001 in 2017.

Ilan Ganot, founder and CEO of Solid Biosciences, commented: “The orphan designations mark a positive step forward in our efforts to advance SGT-001 through development and to patients with DMD in both the United States and Europe. Our teams in the United States and in our new offices in London are working tirelessly to bring our gene therapy candidate SGT-001 to patients as soon as possible.”



EXPERT PICK

Solid Biosciences is developing a novel gene therapy treatment, SGT-001, for Duchenne muscular dystrophy (DMD) and plans to start clinical development in 2017. The approach adopted by the company overcomes one of the key challenges for gene therapy in DMD: the size of the gene. The gene encoding dystrophin, the defective protein in DMD, is the largest in the human genome and is too large for traditional vectors; by using a transgene encoding micro-dystrophin, a truncated form of dystrophin, the problem of transgene size is overcome. Many challenges remain, not least the intramuscular route of administration, whether the truncated dystrophin protein will be effective in patients and the crowded development space in DMD. Nevertheless, being granted Orphan Drug Designation in both the USA and Europe is an important milestone, validating its preclinical package of data. – Richard Philipson



ORGANOVO INITIATES PRECLINICAL DEVELOPMENT OF 3D BIOPRINTED LIVER

Organovo Holdings, Inc., a 3D biology company specialized in the development of 3D human tissues for use in medical research and therapeutic applications, has announced its plan to develop 3D bioprinted human liver tissue for direct transplantation to patients.

The company intends to initiate a preclinical development program based on its achievement of positive results in preliminary preclinical studies in animal models, which showed significant engraftment, vascularization and sustained functionality of its bioprinted liver tissue. The engrafted liver tissue also showed stable expression of liver-specific proteins and metabolic enzymes.

Organovo intends to submit an Investigational New Drug (IND) application to the FDA for its therapeutic liver tissue in 3–5 years.

The company will also pursue breakthrough therapy designation and clinical development outside the USA to help accelerate time to market.

Keith Murphy, Organovo's CEO, commented: "We're excited to introduce an implantable bioprinted liver tissue as the first preclinical candidate in our therapeutic tissue portfolio, and see the early results as extremely promising. Advancing our first therapeutic tissue into preclinical development is an important milestone for Organovo, and it speaks to the power of our technology platform in addressing multiple applications, including preclinical safety, disease modeling and tissue replacement products for surgical implantation. We believe that 3D bioprinted tissues have an opportunity to provide options for patients who suffer from liver disorders."



ATARA BIO'S EPSTEIN-BARR VIRUS-SPECIFIC CYTOTOXIC T CELLS GAIN ACCESS TO EMA'S PRIME SUPPORT

Atara Biotherapeutics, a California-based biopharmaceutical company, has announced that its allogeneic Epstein-Barr virus (EBV)-specific cytotoxic T lymphocytes (CTL) has gained access to the European Medicines Agency (EMA)'s Priority Medicines (PRIME) support for the treatment of EBV-associated post-transplant lymphoproliferative disorder (EBV-PTLD).

PRIME is a new EMA initiative to provide enhanced scientific guidance and support accelerated review of novel investigational therapies.

EBV-CTLs are a third-party, donor-derived, 'off-the-shelf' T-cell product candidate designed to target and destroy EBV-infected lymphoma cells. It was granted Breakthrough Therapy Designation by the FDA in 2015 for the treatment

of patients with rituximab-refractory, EBV-PTLD following allogeneic hematopoietic cell transplant (alloHCT). AlloHCT is a transplant

of bone marrow stem cells from one person to another as a means to treat a variety of serious diseases, primarily blood cancers.



Atara Bio continues to make strides in its regulatory strategy and was granted PRIME regulatory support by the EMA for its HLA-matched, allogeneic T-cell immunotherapy product targeted to EBV infection following hematopoietic stem cell transplant. The company was previously granted a Breakthrough Therapy Designation by the FDA. While HSCT has been a regular

procedure for decades now, and can cure patients with leukemia and lymphoma, there remains a substantial amount of unmet need in the space related to GVHD and post-transplant infections while patients are temporarily immune-compromised. Atara is one of many companies seeking to improve prognosis following HSCT, as industry begins to investigate the full potential of HSCT for blood cancers and beyond. – Mark Curtis



SPARK PROVIDES EFFICACY & DURABILITY DATA OF ITS GENE THERAPY TRIAL

Spark Therapeutics, a US-based gene therapy company, has announced efficacy and durability data of its Phase III trial of Voretigene Neparvovec for the treatment of inherited retinal diseases caused by mutations in the *RPE65* gene.

Data was presented by the principal Investigator of the study, Dr Albert Maguire of the University of Pennsylvania, at the American Academy of Ophthalmology 2016 annual meeting in Chicago. Results included 1-year efficacy data from the crossover group and 2-year durability data from the original intervention group.

Voretigene neparvovec employs an adeno-associated virus-mediated gene therapy to restore, halt or slow the decline of patient's vision caused by mutations in *RPE65*. It has received both breakthrough therapy

and orphan product designations from the FDA, as well as orphan product designation from the EMA.

The present Phase III trial of voretigene neparvovec is a randomized, controlled, multicenter trial conducted in 29 subjects with confirmed *RPE65* gene mutations. The original intervention group consists of 20 subjects and 9 subjects in the control group. Voretigene neparvovec was administered to both the eyes of 20 subjects in the intervention group. After 1-year of undergoing the same retinal and visual function testing as the intervention subjects, all 9 subjects in the control group elected to crossover and receive voretigene neparvovec in both eyes. The modified intent to treat population (n = 29) includes all subjects who received voretigene neparvovec, either in the original

intervention group or in the crossover group of the Phase III trial.

Data showed that the nine crossover subjects displayed significant improvement on the primary endpoint, measured in change of a multi-luminance mobility test between baseline and 1-year. Follow-up data on the original intervention group showed the durability in the Phase III intervention group. No serious adverse events associated with voretigene neparvovec were observed in the study.

Dr Maguire commented: “Results from the ongoing Phase III trial of voretigene neparvovec show that 93% of subjects, including those in the original control group who crossed over to receive intervention, demonstrated a gain in functional vision, and maintained that improvement over 1-year following the procedure. Additionally, the original intervention group sustained its year 1 improvement at year 2. These data further bolster the growing dataset supporting voretigene neparvovec.”



ONES TO WATCH

Spark Therapeutics continues to release data from its Phase III trial of voretigene neparvovec for the treatment of inherited retinal diseases caused by mutations in the RPE65 gene. The data support durability in response at follow-up 2 years after the original treatment and provide further en-

couragement that this approach can produce sustainable improvements in vision in selected patients. Whilst the population amenable to this treatment will be small (an estimated 3,500 individuals in the USA and five major European markets), the company has another AAV-based clinical program in hemophilia B, which is making good progress in a Phase I/II clinical trial, with early evidence of benefit in the first 4 patients treated. Positive clinical data coupled to a solid management team makes this company one to watch.
– Richard Philipson



LICENSING AGREEMENTS & COLLABORATIONS



ADAPTIMMUNE TO COLLABORATE WITH MERCK IN THE FIGHT AGAINST MULTIPLE MYELOMA

Adaptimmune has entered a clinical trial collaboration agreement with Merck to evaluate Adaptimmune's NY-ESO SPEAR® T-Cell Therapy in combination with Merck's KEYTRUDA® in multiple myeloma patients.

Under the terms of the agreement, Adaptimmune will sponsor the clinical trial, which is expected

to begin in the first half of 2017. The study will evaluate the safety, pharmacokinetics, pharmacodynamics and preliminary efficacy of the combination of NY-ESO SPEAR® T-Cell Therapy and anti-programmed death-1 (PD-1) inhibitor, KEYTRUDA® (pembrolizumab) in patients with multiple myeloma. The agreement also includes

provision for potential expansion to include Phase III registration studies in the same indication.

Adaptimmune Therapeutics is a clinical-stage biopharmaceutical company specialized in developing cancer immunotherapy products based on its Specific Peptide Enhanced Affinity Receptor (SPEAR) T-cell platform. Its NY-ESO SPEAR T-cell therapy has previously been evaluated in a Phase I/II trial of multiple myeloma in which 91% of patients had shown a positive response at day 100 post-autologous stem cell transplant. Merck (known as MSD outside USA and Canada)'s KEYTRUDA is a humanized monoclonal antibody that blocks the interaction between PD-1 and its ligands, thereby activating T lymphocytes and potentiating anti-tumor activity.

Dr Rafael Amado, Adaptimmune's CMO, commented: "We have seen encouraging evidence of antitumor effect, safe administration and prolonged persistence of transduced cells in initial single-agent studies of our NY-ESO SPEAR T-cell therapy in patients with advanced myeloma. KEYTRUDA has shown preliminary evidence of activity in multiple myeloma, and there is preclinical evidence to support the view that the combination of NY-ESO SPEAR T-cell therapy and anti-PD1 therapy may lead to meaningful anti-tumor activity. We look forward to evaluating our therapy alone and in combination with KEYTRUDA in a randomized trial of patients with multiple myeloma who are refractory or have relapsed with standard therapy."



MeiraGTx COLLABORATES WITH WCM & LSU TO ADVANCE GENE THERAPY FOR ALS

MeiraGTx, a gene therapy company focusing on the development of gene therapy for acquired and inherited disorders, has announced the expansion of its gene therapy program to treat amyotrophic lateral sclerosis (ALS).

MeiraGTx has entered research collaboration agreements with Weill Cornell Medicine (WCM) and Louisiana State University (LSU) to develop gene therapy platforms to treat ALS patients. The cellular protein TDP-43 is dysregulated in majority of ALS patients. Research in the laboratory of Professor Gregory Petsko (WCM) has discovered the role of nonsense-mediated decay (NMD) pathway, one of cell's

quality control mechanism, in alleviating the TDP-43 mediated toxicity in ALS models. Their research has also shown that increased expression of UPF1, the master regulator of NMD, has neuroprotective effect from TDP-43 mediated toxicity. In collaboration with LSU's Professor Klein, the company will conduct preclinical studies to evaluate the efficacy of a UPF1-based gene therapy in ALS animal models.

Dr Alexandria Forbes, the CEO of MeiraGTx, commented: "We are very excited about our work with Dr Petsko and Dr Klein, leaders in the field of neurodegeneration, to develop a gene therapy

targeting TDP-43 dysfunction in ALS. We believe that this may lead to not only an important new therapeutic approach, but further investigation of the genetic causes of ALS will provide insight for the development of additional gene therapies to treat this and other devastating neurodegenerative diseases.”



HEMACARE SIGNS DISTRIBUTION AGREEMENT WITH KOREA-BASED ACCURESEARCH

HemaCare Corporation, a cell therapy solutions service provider, has entered into a distribution agreement with Seoul-based AccuResearch Korea, Inc. The agreement aims to support researchers in South Korea with HemaCare’s cell products, for their scientific research and development needs. Researchers will be able to access both fresh and cryopreserved cells through direct shipments from HemaCare’s FDA-registered donor collection center as well as its cell isolation laboratory in California,

and also receive customer service and technical support from HemaCare.

Pete van der Wal, HemaCare’s CEO, commented: “Our cell and tissue collection expertise, registry of highly profiled, recallable donors, extensive capabilities in cell processing, cold chain logistics management, and professional consulting services makes HemaCare a partner of choice to support the unique needs and requirements of worldwide scientific and cell therapy researchers”.



TXCELL COLLABORATES WITH UNIVERSITY OF BRITISH COLUMBIA TO ADVANCE CAR-TREGS

TxCell, a clinical-stage biotechnology company specialized in the development of personalized T-cell immunotherapies using regulatory T cells (Treg) for the treatment of severe chronic inflammatory and autoimmune diseases, has announced the initiation of its strategic R&D collaboration agreement with the University of British Columbia (UBC) in Canada. The collaboration aims to evaluate the potential of CAR-Treg cells in preclinical models of solid organ transplantation.

Regulatory T cells have already demonstrated the potential to address transplant rejection, a major challenge in transplantation. This collaboration between TxCell and the UBC team is the result of a recently published first proof-of-concept study with human HLA-A2-specific CAR-Treg cells in a preclinical model of transplantation by UBC’s Professor Megan Levings.

The collaboration will cover the development of a CAR-Treg-based cellular immunotherapy for

the prevention of graft rejection in solid organ transplantation. Under the terms of the agreement, UBC will conduct non-clinical pharmacology studies with CAR-Treg cells under the leadership of Professor Levings and will aim to initiate a first-in-man study in transplantation patients as soon as possible. TxCell has an exclusive option on programs and products developed under this agreement. The financial terms of the collaboration have not been disclosed yet.

Arnaud Foussat, the Senior VP, Corporate Development and Head of External Collaborations and Alliance Management of TxCell, commented: "The recent *in*

vivo proof-of-concept published by UBC in a leading international scientific journal is a critical milestone in the pioneering field of CAR-Treg cells. In contrast to existing approaches based on polyclonal Tregs already tested in clinical trials, we have chosen to bring antigen specificity through a CAR, with the aim of increasing the potential to address the vast unmet medical need in transplantation. We are honored that Professor Levings has chosen TxCell as its partner for this program and we are looking forward to our collaboration towards a common goal of initiating a first-in-man study as rapidly as possible."



BRAINSTORM'S STEM CELL TECHNOLOGY RECEIVES US PATENT

BrainStorm Cell Therapeutics, a biotechnology company focusing on the development of stem cell therapies for neurodegenerative diseases, has announced that the US Patent and Trademark Office has granted US patent for NurOwn®, its proprietary mesenchymal stem cells for the treatment of CNS diseases.

The allowed patent claims cover mesenchymal stem cells that secrete neurotrophic factors, including brain-derived neurotrophic factor and glial derived neurotrophic factor, as well as pharmaceutical compositions that are made up of these factors.

BrainStorm develops adult stem cell therapies from autologous bone marrow cells for the treatment of neurodegenerative diseases.

NurOwn was developed by the company in collaboration with its chief scientist, Professor Dani Offen of Israel's Tel Aviv University.

BrainStorm's CEO Chaim Lebovits, commented: "This patent for NurOwn®, our differentiated mesenchymal stem cells, for use as a pharmaceutical along with the previously granted patents and patent applications, is part of our strategy to aggressively establish a broad portfolio of intellectual property to protect all of our commercially important discoveries."



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PROMETHERA RAISES 10 MILLION EUROS IN SERIES C-EXTENSION FINANCING

Promethera Biosciences, a Paris-based clinical-stage biotechnology company focused on the development of cell therapies for liver diseases, has raised 10 million euros in a Series C-extension financing.

The funds will provide support for Promethera to expand its product portfolio to include larger liver disease indications such as acute-on-chronic liver failure, nonalcoholic steatohepatitis and fibrosis and to

advance these developments towards the clinic.

All major existing shareholders including Vesalius Biocapital, SRIW, Fund+, MGI Global Fund, Boehringer Ingelheim Venture Fund and SMS Investments participated this round. New investors, Mitsubishi UFJ Capital Co., Ltd and Cell Innovation Partners, L.P. (CIP) from Japan and LifeLiver Co., Ltd from South Korea also joined the financing round.



LION APPOINTS GREGORY SCHIFFMAN AS CFO

Lion Biotechnologies, a clinical-stage biopharmaceutical company specialized in the development of tumor infiltrating lymphocytes-based cancer

immunotherapies, has announced the appointment of Gregory T Schiffman as its Chief Financial Officer.

Mr Schiffman has 15 years of experience in the healthcare industry and joins Lion from StemCells,

Inc., where he was the Executive Vice President and CFO. Prior to that, he was the Executive Vice President and CFO of Dendreon Corporation. He has also held various financial positions at Affymetrix and Applied Biosystems.

LYSOGENE APPOINTS MARK PLAVSIC AS CTO

Lysogene, a US-based biopharmaceutical company focusing on the development of gene therapy technology for CNS diseases, has appointed Dr Mark Plavsic, as its new CTO. This move is part of Lysogene's strategic plan to expand senior leadership in the USA to support its international

development. Dr Plavsic has more than 30 years of experience in process and analytics development and manufacturing and will be based in the company's US office in Cambridge MA, reporting directly to Karen Aiach, Lysogene's CEO and founder. His industry expertise is hoping to support

Lysogene's gene therapy of neurodegenerative diseases.

Dr Plavsic joins Lysogene from Torque Therapeutics where he was the head of process development and manufacturing. Prior to that Dr Plavsic held multiple positions at Sanofi Genzyme, Astra Zeneca and Invitrogen Corporation.