

Commercial insight: cell and gene therapy

JUN
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 promising early clinical data announced by AGTC for its treatment for X-linked retinoschisis, and by Ziopharm for its advanced glioblastoma treatment. The treatments, which both use

AAV-based vectors, appear to be well tolerated in their respective Phase 1 trials, with the Ziopharm med also showing early evidence of dose-dependent pharmacodynamic effects. On the manufacturing front, CRISPR Therapeutics has reached an agreement with MaSTherCell SA, which will manufacture CRISPR's CAR-T therapies; there's also relief for AveXis, which has reached alignment with FDA regarding compliance with GMP for its manufacturing process for its spinal muscular atrophy treatment. Finally, this month brings a new player to the CAR-T table, with news from Nanjing Legend that treatment with its therapy targeting BCMA for multiple myeloma resulted in an impressive 94% remission rate within 2 months of treatment, albeit with a high frequency of symptoms of cytokine release. Novartis and Kite Pharma are clearly not going to have things all their own way!



GENE THERAPY
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CELL THERAPY
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CELL THERAPY: NantKwest announced expansion of its oncology program focused on the use of natural killer (NK) cells. The company's platform has three pillars, two of which involve engineered versions of NK cells to deliver antibody or chimeric antigen receptor (CAR)-mediated cell death. Interestingly, while its therapies are still being administered in a second line setting following disease progression, the new studies being initiated by the company combine its immunotherapies with low-dose chemotherapy and radiation, rather than as stand-alone therapy. As we progress with the development of cell-based immunotherapies, it is becoming increasingly evident that a multi-faceted approach will be necessary to combat solid tumor indications in the clinic, wherein several therapeutics tools are deployed in tandem. Investigating immunotherapies in conjunction with chemotherapeutics may provide insight into how we may best bring cell-based immunotherapies into a first-line combination setting.



BLUEBIRD BIO ANNOUNCES TOPLINE INTERIM CLINICAL DATA FROM STARBEAM STUDY OF LENTI-D™ DRUG PRODUCT IN CALD

Topline interim data indicating the surpassal of the trial's primary endpoint has been released from bluebird bio's Phase 2/3 Starbeam Study (ALD-102) evaluating the Lenti-D™ investigational autologous therapy in boys under 18 years old with cerebral adrenoleukodystrophy (CALD).

CALD is characterized by a breakdown of the protective sheath of the nerve cells in the brain that are responsible for thinking and muscle control. Current treatment for the condition is allogeneic hematopoietic stem cell transplant (HSCT), but this carries the risks of graft-versus-host disease (GvHD), as well as opportunistic infections and the lack of suitably matched donors. Instead, Lenti-D transplant patients with their own cells

that have been modified to contain functional copies of the *ABCD1* gene. This gene addition should result in the production of functional adrenoleukodystrophy protein (ALDP), a protein critical for the breakdown of very long chain fatty acids (VLCFAs), build up of which contributes to neurodegeneration in CALD.

17 patients have completed 2 years follow-up of the Starbeam study, resulting in 88% remaining free of major functional disabilities, thus achieving, and exceeding, the primary endpoint of the trial. No patients treated with Lenti-D had GvHD, and there was no graft rejection or clonal dominance. The trial is due to be expanded prior to regulatory filings and potential manufacturing in Europe.



PEDIATRIC DISEASE DESIGNATION FOR FIBROCELL'S SCELORDERMA CANDIDATE

Fibrocell's scleroderma gene therapy has been granted Rare Pediatric Disease Designation by the FDA. The company will thus be able to expedite the review process for future Biologics License Applications (BLA) submissions. This is due to the Rare Pediatric Disease Priority Review Voucher program that is part of the designation.

Scleroderma is a chronic autoimmune disease that is characterized by the excess production of extracellular matrix. This can impair growth, development and movement as well as resulting in severe joint pain from lesions. Fibrocell's gene candidate for this condition, FCX-013, comprises of genetically modified fibroblast cells that are injected at fibrosis sites. FCX-013 has a biologic switch incorporated within it (Intrexon's proprietary RheoSwitch Therapeutic System®), this is activated by an orally administered compound, which initiates the expression of a

collagen that breaks down excess collagen accumulation. Halting the oral compound stops protein production once the fibrosis has been sufficiently treated.

"We are pleased the FDA has awarded Rare Pediatric Disease Designation to FCX-013, which in addition to its Orphan Drug Designation provides important incentives to Fibrocell for developing therapies for rare pediatric diseases," commented CEO John Maslowski. "Moderate to severe forms of localized scleroderma, including the linear subtype, can result in significant morbidity, including pain, restricted motion, disfigurement and developmental issues. With no FDA-approved therapies available, we believe controlled gene therapy through FCX-013 offers promise to address this high unmet medical need of patients suffering from this chronic and often debilitating disease."



ENCOURAGING UPDATES FROM CELYAD'S CAR-T TUMOR TRIAL

Celyad is developing a unique chimerical antigen receptor (CAR)-T cell platform, using natural killer receptor (NKR) transduced on to T lymphocytes. As an advantage over traditional CAR-T therapies, natural killer (NK) cell receptors enable a single receptor to recognize multiple tumor antigens. CAR-T NKR-2, is a CAR-T-cell engineered to

express the human NKR, NKG2D, which is an activating receptor. CAR-T NKR-2 triggers cell killing through the binding of NKG2D to any of eight naturally occurring ligands that are known to be over-expressed on more than 80% of tumors. A multitude of mechanisms come together to make NKR-2 a potent long-term immunotherapy

including the disruption of blood supply to tumors and the recruitment of supplementary anti-tumor cells. Celyad's approach does not use chemotherapy pre-conditioning, allowing the patient's immune system to remain intact.

The initial results show that two colorectal cancer (mCRC) patients, whose disease was still progressing after at least two prior chemotherapy regimens, achieved a confirmed stable disease (SD) according to RECIST criteria at 3 months. Toxicity

signals were not observed in any patients. A third of pancreatic cancer patients enrolled in the trial is still experiencing progression to date.

Christian Homsy, CEO of Celyad, commented: "We are pleased to have observed these encouraging preliminary results in such a late stage population. Despite being dosed only at a tenth of the expected efficacious dose based on animal experiments, the results show a stabilization of the disease. We look forward to the next stages of the trial."



POSITIVE SAFETY PROFILE FROM AGTC'S PHASE 1/2 XLRS STUDY

An encouraging safety profile has been highlighted from the topline data of Applied Genetic Technologies Corporation's (AGTC) Phase 1/2 X-linked retinoschisis (XLRS) trial.

The clinical trial follows patients who have been treated with the company's adeno-associated virus (AAV) based investigational gene therapy. XLRS is a monogenic, inherited condition that is characterized by abnormal splitting of the layers of the retina. This is caused by mutations in the *RS1* gene, affecting the expression of the protein retinoschisin. It is hoped that this new gene therapy approach will address the as of yet unmet medical need of XLRS

patients whose condition can result in legal blindness by adulthood.

Results from the dose escalation trial showed in 12 patients enrolled, most experienced mild ocular inflammation that was successfully controlled with corticosteroids, whilst no subjects experienced any adverse effects. The treatment was considered to be generally well tolerated.

CMO Michael Goldstein said of the results that the company is "continuing enrollment at the highest dose in the expansion group and look forward to providing additional updates with respect to safety, potential efficacy and biologic activity endpoints".



BELLICUM ANNOUNCES CLINICAL RESULTS OF BPX-501 IN PEDIATRIC LEUKEMIAS

Bellicum has presented the results from their pediatric leukemia clinical trial. Investigating the use of

the adjunct T-cell therapy, BPX-501, highlights from the data include rapid immune reconstitution,

low incidence of acute and chronic GvHD, and a low rate of disease relapse.

BPX-501 comprises of engineered donor T cells, which incorporate Bellicum's CaspaCIDE® safety switch. This facilitates the elimination of alloreactive BPX-501 T cells (via administration of activator agent rimiducid) should uncontrollable GvHD occur. Intended for administration after an allogeneic hematopoietic stem cell transplant (HSCT), the therapy enhances immune reconstitution and viral infection control.

Trial results, which were presented at the 22nd Congress of the European Hematology Association, showed that the administration of BPX-501 to 47 children with high-risk acute lymphoblastic leukemia following a T-cell depleted

haploidentical HSCT resulted in just 11% grade 2–4 GvHD, and 4.7% for grade 3–4. Infusions of rimiducid were shown to increase the expansion of infection-fighting BPX-501 cells. The results collected have been deemed favorable when compared to historic controls.

CEO Rick Fair stated: “We are pleased by the profile observed with BPX-501 in pediatric patients receiving a haploidentical transplant, and by its potential to reduce disease relapse. These results provide important insights into the potential long-term benefits of BPX-501, and support our plans to begin a mid-stage study this year in adults with hematologic cancers, for whom lack of a matched donor and disease relapse are significant treatment challenges.”



VOYAGER THERAPEUTICS SELECTS LEAD CLINICAL CANDIDATE FOR HUNTINGTON'S DISEASE

Voyager Therapeutics has announced the selection of a lead gene therapy candidate for the treatment of Huntington's disease. Composed of an adeno-associated virus (AAV) capsid and proprietary transgene, the candidate VY-HTT01 will be developed in collaboration with the CHDI foundation, a non-profit organization that aims to advance therapies, which slow the progression of Huntington's disease. The candidate was selected and optimized in collaboration with researchers from Sanofi Genzyme.

Huntington's disease is an inherited, neurodegenerative condition that is eventually fatal. It is caused by an expansion mutation in the *HTT*

gene that subsequently affects motor and cognitive abilities. Voyageur's VY-HTT01 therefore includes a transgene which harnesses the RNA interference pathway to selectively knock down the production of *HTT* messenger RNA (mRNA), thus downregulating the expression of *HTT*. Preclinical studies of VY-HTT01 in non-human primates resulted in a significant suppression of *HTT* mRNA of more than 50%. The vector genome was selected following extensive optimization and is considered a good candidate for manufacturing scale up.

Further preclinical and pharmacological studies of VY-HTT01 have begun with a view to submitting an

investigational new drug (IND) application in 2018. This would then advance the therapy to the Phase 1 trialling stage in which patients would be treated with a single administration to the brain.

CHDI president Robi Blumenstein expressed that the foundation “is delighted to be collaborating with Voyager, a leader in developing gene therapy programs for severe neurological diseases.”



AVEXIS ALIGNS WITH FDA ON GMP MANUFACTURING OF SMA GENE THERAPY

AveXis has aligned with the FDA regarding the compliance of its manufacturing process for gene therapy AVXS-101 with Good Manufacturing Practice (GMP). This benchmarks FDA support for the company’s manufacturing route, carried out at their own facility, for the commercial manufacture of the proprietary candidate. The initial product made at the facility is planned for use in two upcoming trials of AVXS-101 in patients with varying types of Spinal Muscular Atrophy (SMA).

The final remaining caveat from the FDA is the full implementation of its potency assay qualification plan, prior to the initiation of upcoming clinical studies. Currently, the FDA has commented that not enough information regarding these has been provided to assess the feasibility of the plans. The relevant data is expected to be ready by August this year.

AVXS-101 is a gene therapy that targets the underlying monogenic cause of SMA, and is effective in crossing the blood–brain barrier, thus facilitating an intravenous route of delivery and effective targeting.

CEO Sean Nolan commented that the meeting was successful in cooperating with the FDA on “commercial manufacturing process, analytical methods and comparability protocol, all three of which we believe were achieved in this collaborative and constructive discussion.” He further stated, “We are pleased with the outcomes of the meeting and the progress we have made at the AveXis facility, and, most importantly, believe we have a scalable GMP commercial process in place to fulfill future patient demand and a path forward to potentially utilize the Phase 1 data in our regulatory pathway.”



AFFIMED PRESENTS DATA NK MULTIPLE MYELOMA TREATMENT

Pre-clinical trials by Affimed have found that the company’s NK candidate, AFM26, results in more potent

cell lysis than both daratumumab and elotuzumab, two monoclonal antibodies (mAbs) currently

approved for myeloma treatment. The treatment is being developed for multiple myeloma (MM).

Affimed's candidate is a bispecific antibody that binds to tumor-specific B-cell maturation antigen (BCMA) on MM cells and to CD16A on NK cells; specifically directing NK-cell anti-tumor activity towards cells expressing BCMA. As NK cells are the first lymphocyte population to re-appear after approved chemotherapy or autologous stem cell transplant treatments, they are a natural target for utilization against minimal residual disease (MRD) in the short window following a transplant. Results also found that AFM26 is

largely unaffected by immunoglobulin, which usually competes with traditional mAb treatments for NK binding. A low cytokine release count further implicated a positive safety profile for AFM26.

CSO Martin Treder commented: "NK cells have been described to play a major role in the control of multiple myeloma; however the recognition and elimination of malignant cells remain challenging. Our bispecific tetravalent NK-cell engager AFM26, a targeted therapeutic specifically binding BCMA on tumor cells, promises to address this need by unlocking NK-cell cytotoxicity in myeloma."



POSITIVE TRIAL UPDATES FROM ZIOPHARM'S GLIOMA GENE THERAPY AT ASCO

A gene therapy highlight from the latest American Society of Clinical Oncology (ASCO) annual meeting was an update from Boston-based biopharm company Ziopharm. The latest results from the company's Phase 1 trial of its combinatorial therapy Ad-RTS-hIL-12 + veledimex in advanced glioblastoma patients is beginning to present a clear correlation between the treatment and survival, as well as a positive safety profile.

Ad-RTS-hIL-12 comprises of an adeno associated virus (AAV) vector engineered to express hIL-12 (INXN-2001). IL-12 is a protein that may improve the body's natural response to disease by enhancing the ability of the immune system to kill tumor cells and interfering with blood flow to the tumor. In Ziopharm's study, this gene therapy

is being investigated in conjunction with oral veledimex, an activator ligand that mediates the expression of IL-12.

Results were reported from 25 patients with recurrent or progressive grade III or IV glioma enrolled in three veledimex dosing cohorts. Median survival from this cohort currently stands at 12.5 months, with the trial ongoing until December this year. A strong, dose-dependent correlation between veledimex dose, veledimex blood-brain barrier penetration, IL-12 and IFN- γ production was observed. The ratio of CD8⁺/FOXP3⁺ (effector/suppressor) T cells measured in peripheral blood 14 to 28 days after viral injection correlated with immune activation by the therapy.

On these latest results, Harvard Medical School Neurosurgery

professor Antonio Chicoca commented: “These data suggest that intra-tumor expression of IL-12 is well tolerated by patients with recurrent glioblastoma. There are also highly encouraging observations

that activation of the immune system in the patients may result in anti-tumor effects. I look forward to understanding Ad-RTS-IL-12 + veledimex’s full potential in this challenging disease in a larger study.”



9-MONTH FOLLOW-UP CORROBORATES POSITIVE EARLY RESULTS FOR ASTERIAS’ SPINAL CORD THERAPY

New efficacy results from Asterias’s SCiStar Phase 1/2a clinical trial shows three of six patients have now recovered two levels of motor function and previously announced improvements in arm, hand and finger function at 3 months and 6 months following administration of AST-OPC1 have been confirmed and further increased at 9 months.

The results come from the 10 million dose cohort in the trialing of AST-OPC1 in spinal cord injury patients. Derived from human embryonic stem cells, AST-OPC1 is an oligodendrocyte progenitor population that has been shown to improve hindlimb and forelimb motor function, reduce cavitation and preserve myelinated axons in preclinical trials.

Previous Phase 1 trialing of the therapy returned with no adverse effects and 80% potential efficacy measured by reduced cavitation as seen on MRI scans. Given the encouraging safety profile, the FDA cleared the therapy for targeted trialing in cervical spine injury patients.

Edward Wirth III, Chief Medical Officer, commented: “Gains in motor function, such as the improvements observed in the SCiStar study to date, have been shown to increase a patient’s ability to function independently following complete cervical spinal cord injuries. We are increasingly encouraged by these continued positive results, which are remarkable compared with spontaneous recovery rates observed in a closely matched untreated patient population.”



EXPERT PICK

We continue to see intriguing data from Asterias Biotherapeutics’ clinical program in spinal cord injury. The company previously reported meaningful improvements in motor function in patients that received 10 million AST-OPC1 cells (oligodendrocyte progenitors). The company now reports

that, after a median duration of 9 months, 50% (n = 3) of patients have recovered two levels of motor function in arm, hand, and finger movement. The company is closely observing a cohort of closely matched untreated patients to make a comparison with spontaneous recovery rates. - Mark Curtis



SPOTLIGHT ON NANJING LEGEND THANKS TO CAR-T BCMA DATA

The ASCO annual meeting shed light on the previously under-the-radar firm Nanjing Legend Biotech who presented impressive chimeric antigen receptor T-cell (CAR T) data from an early phase clinical trial at the meet. The company's cell product LCAR-B38M is being trialled in patients with relapsed and/or refractory multiple myeloma and initial results indicate that the treatment could send the cancer into remission.

Like competitor bluebird bio, Legend Biotech's CAR T therapy targets the B-cell maturation antigen (BCMA), a protein implicated in the proliferation of multiple myeloma. However, Legend Biotech's product diverges from bluebird's on a structural basis; it comprises of a single CAR with two heavy chain variable domains that target different epitopes on the same BCMA antigen. At trial in China, the product resulted in a 94% remission rate within 2 months of treatment with the CAR T candidate. At 4 months, 14 of 19 patients had achieved stringent complete response (sCR), meaning

there were no detectable plasma cells in the patient's bone marrow or myeloma proteins in the serum or urine. Of these, 5 patients were followed up for a year post-treatment, with all maintaining their sCR status.

The treatment's safety profile saw 85% of patients experience cytokine release syndrome (CRS), a common and potentially dangerous complication of anti-T cell injections. Researchers said the majority of those cases were mild and manageable, with only two grade 3 (severe) CRS occurrences that were successfully treated with tocilizumab. No neurologic side effects have been observed.

This news brought a new player to the CAR T table, currently dominated by Kite Pharma and Novartis. Nanjing Legend Biotech is planning to launch a parallel trial in the USA and is looking for financial and scientific partnerships to back its development. It remains to be seen whether they will opt to license the out of China right to the med, an option not ruled out by the company's CSO.



BEYOND PANCREATIC CANCER: NANTKWEST TO TRIAL VACCINE PROGRAM IN ADDITIONAL CANCERS

NANTKWest has expanded its existing pancreatic cancer vaccine program to include numerous additional tumor types. This will

result in additional clinical trialling of the regimen over multiple disease stages for cancers such as lung, breast, head and neck cancer,

colon, melanoma, ovarian, urothelial, Hodgkins and non-Hodgkins lymphoma, sarcoma, and Merkel cell carcinoma.

NANT's cancer vaccine program is a cell therapy comprised of off-the-shelf NK cells with the endogenous activation of dendritic, T and NK cells. This is aimed at enhancing the innate adaptive immune system of patients and has been designed as part of a novel protocol. The overall regime includes metronomic, low-dose chemotherapy and radiation with molecularly informed, tumor-associated antigen vaccines, together with NantKwest's NK cell therapy, to induce immunogenic cell death while waylaying the toxicities of high dose chemotherapy.

The CEO of the California based next generation immunotherapy company, Patrick Soon-Shiong said of the expansion, "Current

therapeutic approaches to the treatment of cancer are often inadequate to fully activate a patient's immune response. Through the NANT Cancer Vaccine program, we believe we can help facilitate a paradigm shift in cancer care with the first clinical program formulated to incorporate low dose, metronomic chemotherapy and radiation, combined with molecularly-informed tumor associated antigens that are designed to activate dendritic and T cells by adenoviral and yeast vaccine vectors, together with both endogenous (IL-15) and exogenous (off the shelf) activation of NantKwest's NK cell therapy." Furthermore, he added that the expanded treatments would all be "based on a similar treatment protocol and designed to more fully harness the power of the immune system and improve cancer patient outcomes."



BLUEBIRD BIO REBUILDS CASE FOR BLOOD DISORDER GENE THERAPY

Bluebird Bio announced early interim data from the ongoing Northstar-2 (HGB-207) Phase 3 clinical study of LentiGlobin drug product in patients with transfusion-dependent β -thalassemia (TDT) and non- β^0/β^0 genotypes.

Two years ago, Bluebird was hit hard when a trial of its LentiGlobin candidate failed to hit the mark in a clinical trial, mainly because patients had variable responses to the treatment, which forced the company to change the manufacturing process for the drug.

The aim was to increase the number of vector copy numbers (VCN) produced and increase the number of lentiviral vector positive

(LVV+) cells – i.e., those that have had their gene sequence corrected – in the hope of making responses more consistent. That new process has now been put through its paces, with what the company said are encouraging results.

The first of six patients recruited into the NorthStar-2 trial of LentiGlobin in patients with β -thalassemia – which causes severe depletion in red blood cells – was able to completely halt regular blood transfusions within a month of treatment and saw hemoglobin levels return to normal within 6 months.

On the downside, the second patient in the trial showed a lower-than-expected result for a

measure of hemoglobin production and VCN, raising the fear that the patient variability issue has not been wholly resolved. A third evaluable patient came in between the other two on the hemoglobin biomarker. Patients two and three have only been followed for 3 and 2 months, respectively, and as yet there is no data on total hemoglobin and transfusion rates.

“Although early, these data add to the growing body of clinical evidence that indicate that LentiGlobin

may offer a transformative benefit for patients with TDT,” said Alexis Thompson, MD, MPH, Ann & Robert H Lurie Children’s Hospital of Chicago, Illinois and a primary investigator on the study. “Patients with TDT are dependent on a burdensome cycle of transfusion and chelation, and for these patients, gene therapy with LentiGlobin may offer a long-term solution with a one-time therapy that alleviates many of the complications of the current treatment paradigm.”



bluebird bio has released tantalizing early evidence that recent improvements to the LentiGlobin drug product manufacturing process are translating to improved clinical outcomes in patients with transfusion-dependent β -thalassaemia. The new LentiGlobin manufacturing process, which was introduced last year and which is based on the addition of two transduction

enhancers, produces an average three-fold increase in vector-positive cells and vector copy number (VCN) compared to the original process. Whilst it remains too early to draw firm conclusions, outcomes in the first treated patient are encouraging and include normal levels of haemoglobin (13.3 g/dL) at 6 months post-treatment. There remains a long way to go – the target enrolment of the study is 15 adult and adolescent patients and 8 pediatric patients – but the early clinical outcomes are clearly promising. – Richard Philipson



AVEXIS TO LICENSE REGENXBIO VECTOR NAV AAV9 TO TREAT NEUROLOGICAL CONDITIONS

AveXis and Regenxbio have signed a worldwide license agreement for the latter’s adeno associated virus (AAV) vector, NAV AAV9. AveXis intends to use the vector in the development of gene therapies for two rare neurological disorders; Rett syndrome (RTT) and a genetic form of amyotrophic lateral sclerosis (ALS). Both are monogenic conditions.

Under the terms of the license agreement, REGENXBIO will

receive an upfront payment upon execution, ongoing fees, milestone payments and royalties on net sales of products incorporating the NAV AAV9 vector. Pre-clinical data corroborating the efficacy and safety of NAV AAV9-based therapies for RTT and ALS have been generated already. As such, the new agreement facilitates the movement of studies to the Investigational New Drug (IND) enabling stage.



Kenneth T Mills, CEO of REGENXBIO, commented, “This license agreement for our NAV AAV9 vector highlights the strength of our relationship with our existing NAV Technology Licensee, AveXis, and our commitment to bringing important new NAV-based gene therapies to patients with severe diseases with significant unmet medical need”.

AveXis’ CEO Sean Nolan further stated, “Building on our experience and the success we have seen to date with the use of REGENXBIO’s NAV AAV9 vector in our spinal muscular atrophy clinical trials, this new license agreement reflects progress on executing our corporate strategy and our vision of becoming the leader in the treatment of rare and life-threatening neurological genetic diseases.”



CELL MEDICA ACQUIRES CELL & GENE THERAPY CATAPULT SUBSIDIARY

London headquartered Cell Medica have acquired Catapult Therapy TCR Limited, a subsidiary of Cell and Gene Therapy Catapult (CGT Catapult). The company has also initiated a collaboration to establish cell therapy manufacturing for Cell Medica at CGT Catapult’s GMP manufacturing facility in Stevenage.

Catapult Therapy TCR Ltd is a special purpose company set up by CGT Catapult, UCL Business and Imperial Innovation. The company’s technology utilizes autologous T cells to target the WT1 antigen expressed in solid tumors and blood cancers. Cell Medica takes over development of the therapy, WT1-TCR, at the Phase 1/ 2 trialing stage. Treatment of 8 patients has already been completed and a manufacturing process put in place. Cell Medica is planning to initiate

a Phase 1/2 clinical trial with a Dominant WT1-TCR version in late 2018. Development will also include transferring manufacturing to the Stevenage site and designing a commercial scale production process.

The move follows a 2016 investment into TCR. Gregg Sando, CEO of Cell Medica, commented: “Our objective is to show how we can enhance any existing TCR cell therapy with the Dominant TCR technology to create a more effective treatment for patients with solid tumours who otherwise have a very poor prognosis. We are also looking forward to an important collaboration with CGT Catapult to initiate manufacturing at the Stevenage GMP facility where we will work together on scale-up strategies for commercial production.”



MASTHERCELL SA TO MANUFACTURE CRISPR CAR T THERAPY

An agreement has been reached between CRISPR therapeutics and MaSTherCell SA to develop and

manufacture CRISPR’s Chimeric antigen receptor T-cell (CAR T) therapies. As a service contract

development and manufacturing organisation (CDMO), MaSTherCell will take over the development and clinical Good Manufacturing Practice (cGMP) production of CTX101 for use at a clinical scale.

CTX101 is CRISPR therapeutics' allogeneic CAR-T therapy for CD19 positive conditions. CRISPR's proprietary gene editing platform is used to modify T cells thus creating an off-the-shelf cell product. This is a contrast to autologous cell therapies that face difficulties with scale up and application to a broad population.

"The signing of this agreement represents an important milestone for CRISPR Therapeutics as it not

only demonstrates our progress with CTX101, but also lays the foundation for our broader activities and emerging pipeline in the allogeneic cell therapy field," commented Jon Terrett, Head of Immuno-Oncology Research and Translation at CRISPR Therapeutics.

General Manager of MaSTherCell, Denis Bedoret, also commented, "We are looking forward to working with CRISPR Therapeutics. They have made significant progress to date with multiplexed gene editing and this provides a solid platform upon which we can bring to bear MaSTherCell's significant experience in the manufacturing of allogeneic cell therapies".



SAREPTA SIGNS DUCHENNE GENE THERAPY PACT WITH FRENCH NON-PROFIT R&D COMPANY GENETHON

Sarepta Therapeutics has signed an agreement with France's Genethon to jointly develop treatments for Duchenne muscular dystrophy and comes after Sarepta's first FDA approval for DMD with its exon-skipping treatment Exondys 51 (eteplirsen).

Sarepta is looking to tap into Genethon's preclinical microdystrophin gene therapy approach, which can target the majority of patients with DMD. Its current med can only treat certain patients, namely those with the mutation of the dystrophin gene amenable to exon 51 skipping, which affects about 13% of the population with DMD.

Earlier this year the company signed an agreement with the Nationwide Children's Hospital (Columbus, Ohio), which also focuses

on the microdystrophin gene therapy program, as well as another form of gene therapy. An initial Phase 1/2a trial for the microdystrophin gene therapy is due to begin at the end of the year and will be done at Nationwide Children's. It also penned an exclusive license agreement with Nationwide for their Galgt2 gene therapy program, originally developed by researcher Paul Martin. This early-stage program aims to research a potential surrogate gene therapy approach to DMD, whereby the gene therapy looks to induce genes that make proteins that can perform a similar function as dystrophin.

"Our agreement with Genethon strengthens our ongoing commitment to patients and is aligned with our strategy of building the

industry's most comprehensive franchise in DMD," said Ed Kaye, Sarepta's outgoing chief. "This partnership brings together our collective experience in Duchenne drug development and Genethon's particular expertise in gene therapy for rare diseases. We look forward to working with Genethon given their knowledge, large infrastructure and state-of the-art manufacturing capabilities to advance next generation therapies for DMD."

Frederic Revah, CEO of Genethon, added: "Microdystrophin-based

gene therapy is a very promising approach with potential application to a large majority of Duchenne patients. In order to accelerate the development of a treatment, we are very pleased to partner with Sarepta Therapeutics, which has demonstrated commitment and success for innovative therapies for Duchenne muscular dystrophy. This partnership brings together the highly complementary and synergistic expertises of Sarepta and Genethon, to the benefit of the patients."



EXPERT PICK

Sarepta Therapeutics continues to build its Duchenne muscular dystrophy (DMD) pipeline with the announcement of a deal to work together with France's Genethon on the latter's preclinical microdystrophin program. This follows hot on the heels of a deal signed earlier this year with

Nationwide Children's Hospital, also in the field of microdystrophin, and a deal with Summit Therapeutics signed in October 2016, which granted Sarepta European rights to Summit's clinical phase utrophin modulator pipeline. Its current FDA-approved DMD medicine eteplirsen, which was approved last Autumn despite having limited data and a negative AdComm, can only treat a subset of DMD patients, namely those with the mutation of the dystrophin gene amenable to exon 51 skipping, which affects about 13% of the population with DMD. The recent pipeline additions, if successful, will give Sarepta treatment options that can be applied to a much broader population of DMD patients. – Richard Philipson



SORRENTO THERAPEUTICS TO CONTRIBUTE TO CELULARITY FORMATION

Clinical-stage biopharmaceutical company, Sorrento therapeutics, have closed a deal to contribute to the formation of Celularity, Inc.

Sorrento, whose lead product candidates include immunotherapies focused on the treatment of both solid tumors and hematological malignancies will add certain

immuno-oncology and cellular therapy intellectual property and assets to Celularity.

Formed and run by former Celgene Cellular Therapeutics CEO, Robert Hariri, Celularity is currently assembling key assets from a growing number of companies in the cell therapy arena.



Sorrento Therapeutics, an antibody-focused biotech, recently signed an agreement in conjunction with its subsidiary TNK Therapeutics, to form Celularity Inc., a new company that will gain IP rights to several immuno-oncology and cell therapy assets. The company will be led by Robert Hariri, who was most recently CEO of Celgene Cellular Therapeutics. Sorrento and TNK are also affiliated with NantKwest, and will develop NK-based immunotherapies. - Mark Curtis



CYNATA THERAPEUTICS FILES PATENT APPLICATION FOR CANCER STEM CELL TECHNOLOGY

Cynata therapeutics has filed a patent application with IP Australia for the use of its proprietary Cymerus™ mesenchymal stem cell (MSC) technology for cancer therapies. This is the second recent patent filing by Cynata regarding the oncological use of the technology.

The Cymerus system is designed to overcome critical manufacturing challenges related to MSCs. Induced pluripotent stem cells (iPSCs) derived from a single blood donation are used to generate mesenchymal angioblasts (MCAs), a precursor that then is used to manufacture an unlimited number of therapeutic

MSCs. This platform has the potential to create an off-the-shelf source of MSCs, setting new standards for stem cell manufacturing.

“We are thrilled to announce the filing of this patent application, which would strengthen our intellectual property portfolio in the oncology field and expand commercial opportunities for Cymerus in immunotherapy,” said Dr Ross Macdonald, CEO. “Immunotherapy is one of the most exciting areas in oncology and our new intellectual property ensures Cynata is well-positioned to capitalise on future growth in the field.”



\$33 MILLION NK LICENSING DEAL STRUCK BETWEEN CELGENE & DRAGONFLY

In a \$33 million dollar deal, Celgene has acquired the option to license four natural killer (NK) cell-based blood cancer therapeutics from Dragonfly therapeutics. The deal will see the companies collaborating on research and development

to establish NK based treatments as immuno-oncology options, alongside the current favourite T cells.

The platform licensed from Dragonfly, TriNKET™, designs bridges between proteins found on tumour and NK cells. This stimulates NK



cells into attacking the tumor, along with B and T cells and is being considered for a number of hematological conditions including acute myeloid leukemia and multiple myeloma.

This latest move by Celgene follows a history of backing early, discovery-stage biotechs. Dragonfly's considered potential in particular is closely linked with the eminence of its founders and scientific advisory board, that includes a Nobel winner, former director of the National

Cancer institute and White House Cancer Moonshot director.

"NK-cell biology and immunotherapy are increasingly critical areas of hematologic research and we are looking forward to working with Dragonfly's team of world-leading experts," Rupert Vessey, Celgene's president of research and early development, stated. "This collaboration will leverage the strengths of each company as we work together to bring innovative therapies to patients."



\$40 MILLION BACKS GAMIDA'S BREAKTHROUGH UMBILICAL CORD BLOOD THERAPY

Jerusalem-based Gamida Cell has closed their latest financing round with \$40 million of new investment to back the company's Phase 3 trialling of blood cancer cell therapy, NiCord. Lead by new investor Shavit Capital, other participants included VMS investment group, Israel Biotech Fund as well as long-time investor Novartis who bought a 15% stake in the company in 2014.

The primary use of the funding will be the development and commercialization efforts for NiCord, a product derived of umbilical cord blood that is then enriched with stem and progenitor cells. Expanded in culture, the breakthrough designated product acts as a stand-alone graft for patients to whom a fully matched bone marrow donor is not available. Phase 1 and 2

results were published earlier this year and Phase 3 trialling is currently underway as an international and multicenter study; transplantation of the first patient was completed in February this year. As well as trialling, the funding will also support the expansion of Gamida's in-house manufacturing capacity, expansion into the US market, and development of other pipeline products.

Gamida Cell's chair, Julian Adams, commented, "The financing announced today provides important support for Gamida Cell's innovative product pipeline, which has the potential to change the clinical application of cell based therapies. We are excited to take Gamida Cell to the next step towards becoming a commercial global company based on innovative oncology therapy."