Commercial insight: cell and gene therapy

JUL–AUG 2015

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
Alan Boyd
CEO, Boyds, UK

CELL THERAPY
Mark Curtis
Bus. Dev. Analyst, CCRM, Canada

Rahul Sarugaser
VP, Corp. Dev., Hemostemix, Canada

GENE THERAPY: From the past months' news stories it is clear that gene therapy companies and their products are generating a lot of interest, particularly in the investment arena. The IPO window has been open for some time now for companies developing advanced medicines and for the time being it looks like this is going to continue to happen. Big Pharma are also very interested in the sector now as evidenced by the deals being driven by them; this is a very different picture from as recent as 5 years ago. Finally, it is good that the sector is now having to consider the price of gene-based therapies. In my view this is a nice problem to have as a few years ago a discussion about price was way down the agenda, at least publically. Having open discussions about price has only come about due to the fact that gene-based products are getting closer to market and hopefully becoming available to patients – so not such a bad issue to be facing for many reasons.

CELL THERAPY: The biotech industry is currently enjoying tech-like valuations for novel paradigms at early stages of development, including cell-based immunotherapy, *ex vivo* gene therapy, and antibodies targeting cancer stem cells (Stemcentrx, a private pre-clinical company with a $3 billion valuation). Either the innovation is real, or we are in the largest biotech bubble in history. Given the curative potential of these new paradigms and the robustness of platforms in industry, we would argue the former.

PLURISTEM GETS JAPANESE NOD FOR CELL USE IN CLINICAL TRIALS

Pluristem Therapeutics Inc, a leading specialist in placenta-based cell therapies, have received safety clearance from Japan's Pharmaceuticals and Medical Devices Agency, to pursue Phase II clinical trials for their PLX-PAD cells. This recent nod of approval means that Pluristem has received two of three authorizations required before Phase II trials can be conducted.

The company's patented PLX cells are designed to release a number of therapeutic molecules in response to certain stimuli, and thus far, clinical trial data has demonstrated potential for use across multiple indications, the most recent of which is for critical limb ischemia.

Having received safety approval for their PLX-PAD cells, Pluristem are now in a position to consider Phase II clinical trials, via an accelerated regulatory pathway for regenerative medicine, which gives the potential for the cell lines to be approved for use in the event of a successful Phase II trial. All that remains is for Pluristem to gain approval for the clinical trial design - *D Babra*

REASSURANCES FROM KITE PHARMA

Following reports of a patient death in their phase I/II study of KTE-C19 (CD19 CAR-T) treating refractory, aggressive non-Hodgkin's Lymphoma, Kite Pharma have released further information which will likely reassure investors.

The patient death had occurred early in the trial (May 2015) and was determined to be unrelated to KTE-C19 therapy. After discussions with the FDA, Kite has continued enrolling and treating patients in the ongoing trial and still remains on track to present data at the Annual American Society of Hematology meeting later this year.

"We are encouraged by the progress of the KTE-C19 clinical trial and excited by the responses we have seen so far. We believe the KTE-C19 clinical findings are in line with previous results demonstrating the potential of this promising therapeutic approach,"

said Arie Belldegrun, Chairman, President and Chief Executive Officer of Kite.

Kite's T-cell receptor (TCR)-heavy pipeline is in continual development and is a huge driver of a valuation gap between Kite and its nearest competitor, Juno. Kite already has six candidates in clinical testing, including a larger Phase II portion and additional Phase II studies of KTE-C19 in B cell lymphoma in line to initiate later this year. - *W Villiers*

DOI: 10.18609.cgti.2015.005

PHASE II DISAPPOINTMENT HITS AVALANCHE'S GENE THERAPY PROGRAM

Avalanche Biotechnologies have pulled the plug on further research into its lead gene therapy candidate, following disappointing results from Phase II clinical trials.

The California-based company's lead therapy, AVA-101, intended as a one-time treatment for wet age-related macular degeneration, was due to enter the Phase IIb stage of clinical research in the latter part of this year. However, a review of their Phase IIa results demonstrated that despite a good safety profile, the therapy offered limited clinical benefit with little progress towards the goal of decreasing retinal thickness.

Last year, Avalanche became one of the higher profile companies in the gene therapy market, having filed the terms for a $102 million IPO. The initial news of the disappointing outcomes saw Avalanche's share prices drop by more than 50%, followed by the departure of CEO Thomas Chalberg shortly thereafter. Avalanche has since decided to return to the lab before attempting further clinical trials, with this news sending Avalanche's shares down a further 30%.

Some investors have even taken Avalanche's bad fortune as a forecast for all ocular gene therapies; Spark Therapeutics, with a number of candidates intended for use in treating rare ocular diseases, saw its stock price fall 10%.

However, despite the misfortune that has befallen AVA-101, the company is continuing preclinical work on AVA-201, also a treatment for wet AMD, and a further two therapies for color blindness. - *D Babra*

AVALANCHE AND SPARK

Avalanche and Spark are both developing gene therapy treatments for eye diseases. Unfortunately Avalanche seem to have run into problems with their treatment for AMD following the release of their latest clinical study results. Spark on the other hand are now facing the issue that when their treatment for Leber's eye disease is approved, what provisions need to be put in place with Insurance Companies and other Healthcare Payors to help spread the costs of the therapy. So why are these companies on my 'ones to watch list'? With Avalanche the interim CEO, Hans Hull has recently stated that the factors that caused the study to fail may include the dosing and administration variability. One of the most difficult aspects of any drug development programme is to get the dose, and in the case of gene therapies, the administration procedure correct. Therefore I hope Avalanche will be willing to share what the problems were in this study so that we could all possibly benefit from finding out for future studies. For Spark, being one of the companies who have a product which is getting closer to market approval, it will be interesting to see how their pricing and payment discussions go as it sets the path for future products - ***Alan Boyd***

SPARK CONSIDERING PALATABLE INSTALMENT PLAN FOR MILLION-DOLLAR DRUG

Spark Therapeutics Inc., has entered into discussion with health insurance firms and drug benefits managers regarding instalment-type payment plans for a new, promising gene therapy for blindness, which has a projected million-dollar price tag.

The therapy, SPK-RPE65, targets the genes directly into the eye to treat rare forms of blindness. Current trials, run by the Children's Hospital of Philadelphia, USA, have shown efficacy in a handful of patients, with half no longer considered legally blind. Final-stage trial results are due at the end of the year.

Historically, access to treatments and drugs with large price tags has been significantly limited; such is the case on a global scale. The new discussions have largely been prompted by the problems accessing high-price treatments, which insurance companies are generally unwilling to pay out for.

In a recent interview, CEO Jeff Marrazzo said that the company is considering staggered payment options, including an option that would spread the costs over an extended period dependent on the effectiveness of the therapy. In spite of these plans and the projections by a number of analysts, Marrazzo has also said that no official price has been set.

Marrazzo, having worked previously on healthcare costs, has said that he is aware of the problems on the side of the insurers, and wants to help fix the problems.

"The opportunity here is that we can have a dialogue that's saying we're willing to take value over multiple years."

He also hopes to have an effective payment plan in place before the drug is approved.

The emergence of curative or transformative cell and gene therapies has caused a number of companies and healthcare providers/insurers to start looking at alternative payment models to help address the high price tags potentially associated with these treatments. Netherlands-based UniQure and Bluebird Bio Inc., of Cambridge, MA, while considering instalment payment options, have also talked about alternative reimbursement ideas. - *D Babra*

CEO Jeff Marrazzo has said that the company is considering staggered payment options, including an option that would spread the costs over an extended period dependent on the effectiveness of the therapy

DOI: 10.18609.cgti.2015.005

MILLION-DOLLAR GENE THERAPY DELAYED AS FDA DEMANDS FURTHER CLINICAL DATA

Having previously expected to gain approval for their new gene therapy, Glybera®, based on data from a single, pivotal clinical trial, UniQure is now having to review its options following demands by the FDA for further clinical data.

UniQure was initially set to begin its US-based clinical trial for Glybera in 2016, and intended to use the data to build their case to enter the US market. However, this new request from the FDA to include additional clinical data with their BLA filing will undoubtedly cause further delays in seeing the gene therapy reach the US market. UniQure CEO, Jorn Aldag, commented that the company is still assessing its options in the USA, and expects to make a decision later this year.

Glybera, the first gene therapy to be approved in the EU, is used in patients with lipoprotein lipase deficiency and stands as UniQure's breakthrough product in terms of entering the pharmaceutical market. A condition of its approval in Europe was a request for follow-up data spanning 6 years, as regulators continue to grapple with how to assess the safety and efficacy of a new product that targets such a small patient population and comes with the hefty price tag of $1.2 million (€1.1 million).

As it stands, UniQure intends to pursue their plans for their US-based clinical trial in the early part of 2016 in order to meet the post-approval criteria for the European market. However, their Stateside ambitions remains uncertain.

The Netherlands-based UniQure is certainly no stranger to setbacks and the news of the FDA's request for more clinical trials resulted in a 14% drop in the price of shares in their NASDAQ listing.

However, beyond Glybera, UniQure have a number of promising gene therapy candidates in their pipeline, including their Hemophilia B and Sanfilippo B programs. The Hemophilia B program, AMT-060, is set to release data from the first-dose cohort from the Phase I/II trial, with the second-dose cohort results due in 2016. Furthermore, Institut Pasteur, with whom UniQure is working in partnership with, plan to release data from a Phase I/II trial of an AAV5-based gene therapy to treat Sanfilippo B, which could be the first proof-of-concept for a gene therapy for a lysosomal storage disease. - *D Babra*

EXPERT PICK

This is an interesting turn of events as UniQure with Glybera appeared to have completed all their studies to support regulatory approval and have even reported the long term data for their studies at around 6 years – so the question now needs to be asked as to why the FDA have suddenly asked for an additional clinical study to be conducted at this point? Two thoughts come to mind – having seen all the data, do the FDA now want additional information to confirm this or do they want new endpoints in the study explored, which are different from the ones in the completed programme. The other issue may be that the FDA want some patients living in the USA to be treated with the product as to date all the Glybera studies have been conducted outside of the USA.

NANTKWEST CLOSES IPO

NantKwest announced the closure of its IPO, which is estimated to have generated around $222.5 million, from the sale of 9,531,200 shares at a price of $25.00 per share. At the same time, NantKwest gained a further $17 million in funds through the sale of 680,000 shares to existing stock holder, Celgene Corporation.

NantKwest, a leading clinical-stage immunotherapy company, focuses on the natural killer (NK) cell, an important member of the innate immune system. NK cells, similar in their function to cytotoxic $CD8^+$ T lymphocytes, have a considerable ability to rapidly identify the presence of, and proceed to remove, stressed cells such as aberrant tumor cells or cells that have become infected with viral pathogens.

NantKwest was also in the news this month announcing a $1 Million Challenge award from the Prostate Cancer Foundation to investigate the prospect of utilizing their NK cell-based therapeutic technology in advanced prostate cancer. In collaboration with Dr Ganesh Palapattu, University of Michigan, and Dr Karen Knudsen, Thomas Jefferson University, the study will seek to target the PSMA protein – specifically expressed in prostate cancer cells – using NantKwest's activated NKs (aNKs) loaded with chimeric antigen receptors (CARs).

At this stage, the study will take a preclinical format, assessing efficacy "our goal is to create and test the preclinical and clinical efficacy of NK cells engineered to express a CAR molecular that directs them to target and kill prostate tumor cells" commented Dr Palapattu. - *D Babra*

Global cell-based immunotherapy valuations are currently priced-to-perfection, which explains Juno's $4 billion market capitalization with six CAR candidates in the clinic at Phase 2 or earlier. However, NantKwest's recent IPO valuation of $2.5 billion stands alone as it moves to complete recruitment for its first candidate in the clinic, an off-the-shelf NK cell therapy for blood cancers.

JUNO THERAPEUTICS REPORTS SECOND QUARTER 2015 FINANCIAL RESULTS

Going from strength to strength, Juno also published reports of positive financial performance over the second quarter of 2015; the biopharmaceutical company ended Q2 2015 with $313 million in cash, reporting $12.5 million in revenue and a GAAP net loss of $66 million (or $0.79 per share). Factoring in the initial stock purchase by Celgene, Juno has pro-forma cash of $1.3 billion.

The Seattle-based company has published data on a number of candidates that demonstrate significant progress, and the FDA clearance of Juno's lead candidate,

DOI: 10.18609.cgti.2015.005

JCAR015, has placed them in a position to begin their first clinical trial. Targeting CD19 in lymphoblastic leukemia, JCAR015 has been given the go ahead to conduct a phase II registration study in relapsed/refractory patients acute lymphoblastic leukemia (r/r ALL). Another candidate, JCAR017, is set to head into phase I for r/r non Hodgkin's Lymphoma (r/r NHL). The first development candidate MUC-16/IL-12 using the companies 'armored' CAR technology will also be entering the clinic in 2H15.

With significant studies already initiated and future trials rising up the 2H15 pipeline, Juno has made the most of their partnerships and key acquisitions. Driving development at a fast pace and in the right direction, Juno is now emerging as a fully integrated immune-oncology company. *- D Babra*

Driving development at a fast pace and in the right direction, Juno is now emerging as a fully integrated immune-oncology company.

OCATA THERAPEUTICS TO RECEIVE $10 MILLION CASH INJECTION IN PURSUIT OF REGENERATIVE OPHTHALMOLOGY THERAPEUTICS

Ocata Therapeutics is set to receive a loan of up to $10 million from the Silicon Valley Bank (SVB). Ocata, a major player with a focus on regenerative ophthalmology therapies, currently has a number of candidates in clinical trials targeting various forms of macular degeneration, and intends to use the funds from SVB to help pursue further clinical trials for their current candidates, as well as the initiation of some pre-clinical studies.

The loan from the Silicon Valley Bank has been set up to be paid in two instalments. The first payment, to the value of $6 million, has already been received. However, at present, the remainder of the money will only be paid in the event that Ocata is able to meet certain clinical and corporate criteria set out by SVB. SVB has a strong history of providing financial aid to biotechnology companies, and both parties have highlighted the additional flexibility and support the funding will provide to ongoing, pivotal programs at Ocata. *- D Babra*

SHARE DROP FOR BLUEBIRD BIO INC

The first half of this month saw increased market volatility that hit a number of biotech companies. Bluebird Bio Inc., developer of gene therapies for rare diseases and cancer, saw further falls in its share listing price as it fell to $133.07 over the course of the month. This came after the company announced that its operating costs tripled in Q2 and its net loss has expanded to $1.57 per share, over double what market analysts had predicted. *- W Villiers*

GENE THERAPY PLAYER, REGENX, SETS OUT FOR $100 MILLION IPO

The Maryland-based biotech, ReGenX Bio – co-founded by gene therapy pioneer and veteran James Wilson – filed the terms of its IPO as it aims to raise $100 million towards pursuing independent R&D.

At present, ReGenX Bio appears intent on using the funds from the IPO to pursue preclinical research around gene therapy for homozygous familial hypercholesterolemia, a rare genetic disorder which causes abnormally elevated levels of bad cholesterol. Further to this, funds raised will also be put towards the company's programs around gene therapy for both Hurler Syndrome and age-related macular degeneration.

ReGenX's technology, which forms the basis for each of their candidates, is a product engine called NAV, using adeno-associated viruses (AAV) as a vector to deliver functional genes to silence disease causing ones. This technology has put the company in a seemingly strong position to push out on its own, given that many of the recent promising startups have licensed technology from ReGenX Bio – ReGenX currently has eight out-licensing deals on file using the NAV technology. Furthermore, ReGenX have recently secured $70.5 million in funds, with new investor, Vivo Capital footing a large chunk of the bill. - *W Villiers*

EXPERT PICK

It is interesting to hear that ReGenX are considering going for an IPO to raise funds for their in-house R&D programmes. ReGenX have been around for a number of years now and clearly have a large amount of experience in the AAV vector space with their specific serotypes, but up until now have not really been considered as a gene-based product development company. It now looks like all this will change if their IPO is successful, as they emerge as a company developing their own products rather than simply supplying the tools for others to do that.

"ICE BUCKET CHALLENGE" FUNDS TO SUPPORT DEVELOPMENT OF NATIONAL ALS DATABASE

Some of the money raised by the Ice Bucket Challenge, which saw over $115 million donated to the ALS Association, is being used to build a database of genetic and clinical traits from 1,500 people with amyotrophic lateral sclerosis (ALS). The database, being built by Biogen in collaboration with Columbia University Medical Center, will be used to help improve the understanding of genetic contributions to the different forms of ALS.

The Biogen–Columbia collaboration is largely being funded by Biogen itself, but the ALS Association has allocated a $3.5 million slice of the Ice Bucket money to the project. In addition, the Massachusetts General Hospital will

DOI: 10.18609.cgti.2015.005

use its NeuroBank system for data collection, and Cedars-Sinai, Los Angeles, have offered services in developing cell lines.

ALS is considered to be an umbrella term for a number of motor neuron diseases, but a great deal remains unknown about the underlying causes and potential treatments or cures. This initiative aims to unveil some of the mystery around ALS, as well as potentially support the design of clinical trials of targeted therapies, which will be further supported by blood samples from ALS patients. Blood cells, taken from these samples, will be stored at Cedars-Sinai at the Induced Pluripotent Stem Cell (iPSC) Core, making them available to scientists and clinical researchers to create cell lines for research.

"By focusing on patients seen by participating ALS clinics, this project will allow investigators to ask how different genetic causes of ALS translate into different clinical consequences" commented ALS Association Chief Scientist Lucie Bruijn, PhD, MBA.

Dhruv Sareen, of Cedars-Sinai, has commented on the project - "The ability to create patient iPS cells from such a genetically well-annotated ALS blood repository will allow us to model causes of motor neuron degeneration in ALS." - *D Babra*

The development of treatments for orphan and rare diseases has increased substantially over the past decade. However one of the problems in treating such diseases is that because many of them do not have clearly defined therapeutics approaches little is known about the natural history of the disease being studied and as such this makes the selection of appropriate and clinically useful endpoints for clinical studies very difficult. So it is good to see that a company, like Biogen, is willing to utilize their resources to help define the natural history of a disease like ALS.

BENITEC PURSUES IPO AMIDST STOCK EXCHANGE DOWNTURN

Australia's Benitec Biopharma picked an unfortunate week to debut on the NASDAQ, timing their introduction with a week that saw the whole of the NASDAQ Biotechnology index drop 4.5%. On August 18th, Benitec's IPO managed to raise $14 million through an offering of 1.5 million American depository shares, however its stock had seen a fall of 13% by the end of the week.

The company, an RNA interference specialist, states that its technology, known as DNA-directed RNAi, overcomes the drawbacks of other gene silencing methods, as well as having the advantage of reduced toxicity and fewer side effects. The patented ddRNAi technology introduces small doses of DNA sequences directly into the nucleus of the cell, causing *in vivo* cells to produce siRNA. According to the company's website, in order to achieve this, a "range of well-characterized gene therapy vectors, viral and non-viral, like lentivirus, adenovirus, AAV or modified polyethylenimine can be used."

Entering the US market, Benitec held an offer price of $9.21 per ADS,

23% less than the offering on the Australian Stock Exchange. However, the cut-price offerings were not enough to overcome what was a bad week for stocks overall. This spin of bad luck is not the first in Benitec's recent financial history, with the company having to scrap plans for terms on a $65 million offering, as recent as June.

Despite setbacks entering the US Stock Exchange, the stage appears to be somewhat set for Benitec, with late-stage trials of a hepatitis C treatment set for the second quarter of 2017, and the ddRNAi platform is being utilized by Calimmune on a candidate in the fight against HIV. - *D Babra*

JUNO GIVEN EARLY GREEN LIGHT FOR BILLION-DOLLAR COLLABORATION WITH CELGENE

A collaboration between Juno Therapeutics, Inc. and Celgene Corporation, to study cures for cancer and autoimmune diseases, has taken effect much earlier than expected, following an announcement that the Federal Trade Commission has allowed an early finish to the waiting period that must be fulfilled as part of the Hart-Scott-Rodino Antitrust Improvements Act of 1976 (HSR Act).

Juno, a biopharmaceutical company, is focused on developing ways of re-activating the body's immune system to fight cancer. The company uses this premise to develop cell-based cancer immunotherapies, technology to which Celgene is making a big commitment.

The deal, which took effect on July 31 and is worth nearly $1 billion, has given Celgene about 10% of Juno's stock, with the option to buy more over time. For the first payment, Celgene has chosen to pay $150 million in cash, with the remainder covered by the purchase of 9,137,672 shares at $93.00 per share. Under the terms of the agreement, in addition to taking hold of a tenth of Juno's stock, Celgene will head up R&D outside of North America, as well retaining the right to choose two products to share costs and profits with Juno. The announcement also included news of the addition of Celgene Head of R&D, Dr Thomas Daniel to the Juno Board of Directors. - *D Babra*

Juno's war chest of $1.31 billion means it won't have to dilute shareholder value for some time to come, and will give the company the legs to move many of its existing clinical candidates through to market. The biotech industry is well aware of the safety concerns associated with first-generation CAR products (cytokine storms), so Juno would be wise to spend some of its cash on engineering second- and third-generation CAR products with improved safety and efficacy profiles. The blood cancer market is flooded with cell-based immunotherapies. No doubt, a good portion of the company's funds will be spent on advancing its WT-1 and L1-CAM programs, which target solid tumors, a necessary move to ensure the long-term success of the company in oncology.

DOI: 10.18609.cgti.2015.005

IMMUNE DESIGN AND GENENTECH TO COLLABORATE ON CLINICAL TRIAL

A clinical trial collaboration between clinical-stage immunotherapy company, Immune Design, and Roche Group member, Genentech, has been announced, as a part of Immune Design's ongoing immune-oncology program. Immune Design, whose technology is designed around antigen-specific cytotoxic T cells and their ability to undergo clonal expansion, have entered into the collaboration to assess the safety and efficacy of a combination of two candidates, Immune Design's lead candidate, CMB305, and atezolizumab, of Genentech, in Phase II clinical trials for soft tissue sarcoma.

Immune Design has already begun Phase Ib trials for CMB305, assessing safety and efficacy as a single candidate. CMB305 is designed to induce the expansion of tumor-specific cytotoxic $CD8^+$ T cells against a specific antigen, which has been identified on a wide range of tumors. With this in mind, the rationale behind the collaboration is from a mechanistic point of view, with the two candidates working synergistically, producing a treatment with greater potency. Atezolizumab, a monoclonal antibody targeted against PD-L1, acts to inhibit certain T-cell checkpoints that normally suppress the T-cell response. Therefore, it is thought that, in combination with CMB305, atezolizumab will allow the expansion of cytotoxic T cells and provide an effective treatment against soft-tissue tumors of an advanced or relapsed nature. - *D Babra*

UNIQURE AND BRISTOL-MYERS SQUIBB FORM GENE THERAPY COLLABORATION

UniQure, also made the headlines this month owing to its partnership with global pharmaceutical firm, Bristol-Myers Squibb (BMS).

BMS has strengthened its gene therapy alliance with UniQure, by increasing its stake in the Netherlands-based company up towards 10%. The deal saw BMS buying an additional 1.3 million shares in UniQure at a cost of $38 million. UniQure netted a further $15 million for the addition of three targets to the cardiovascular gene therapy

"With the recent addition of more than $200 million in capital from our collaboration ...we have the financial resources to meet the needs of our collaboration and advance the development of our proprietary pipeline focused on CNS and liver-directed diseases." Jorn Aldag, CEO, UniQure

collaboration, taking the total cost to BMS, to $53 million.

The exact stake held by BMS, stands at 9.9%, helped by the acquisition of the additional shares. Under the terms of the gene therapy alliance, BMS is able to obtain two portions of UniQure's stock at 5% a piece, with further rights to add up to ten targets into the collaboration; up to now, BMS has added four targets, the last of which prompted the $15 million payout. UniQure stand to gain significant financial stability from the collaboration, having already benefited to the tune of $140 million.

In a recent statement, UniQure CEO, Jorn Aldag commented, "With the recent addition of more than $200 million in capital from our collaboration and the company's recent follow-on offering, we have the financial resources to meet the needs of our collaboration and advance the development of our proprietary pipeline focused on CNS and liver-directed diseases." - *D Babra*

ONCOSEC ENROLS FIRST PATIENT IN CLINICAL TRIAL FOR COMBINATION THERAPY IN METASTATIC MELANOMA

OncoSec Medical Inc. is set to begin a Phase II clinical trial assessing the safety, tolerability and efficacy of its OncoSec's Immunopulse™ IL-12 in combination with Merck's approved PD-1 antagonist, pembrolizumab in metastatic melanoma. The rationale for the combination therapy is based upon the premise that in order for anti-PD-1-targeted therapies to be effective, tumors must demonstrate some form of inflammation and have tumor infiltrating lymphocytes (TILs). Data gleaned thus far, during both preclinical research and clinical studies, has shown that Immunopulse™ IL-12 can increase a patients TIL count, and therefore allow therapies, such as pembrozulimab, to work with greater efficacy.

OncoSec, who are developers of DNA-based intratumoral cancer immunotherapies, is working with the University of California to run the trial, and has enrolled its first patient this month. The trial has plans to enrol around 42 patients with metastatic melanoma with what is described as a "low-TIL" count, with treatment schedules of prebolizumab administered once every 3 weeks, and Immunopulse™ IL-12 being administered at 6-week intervals. - *D Babra*

It was only a matter of time before combinatorial treatment paradigms emerged that blend cell therapy, gene therapy, and immunotherapy. One of the key goals, mechanistically, is to generate cytotoxic $CD8^+$ T-cell responses against cancer cells while simultaneously eliminating tumor blockade – a powerful approach. Immune Design's collaboration to pair its lentiviral-based immunotherapy with Genetech's checkpoint inhibitor atezolizumab, and OncoSec's collaboration to investigate its plasmid-based ImmunoPulse IL-12 therapy with Merck's pembrolizumab continue to play into this trend. Combinatorial regimes, like these, will buoy the CAGR of the immunotherapy industry for some time to come.

DOI: 10.18609.cgti.2015.005

AGTC-BIOGEN COLLABORATION MEETS MILESTONE IN XLRS STUDY

Applied Genetics Technologies Corporation (AGTC), a biotechnology company renowned for their strong product pipeline has announced it has met a patient enrolment milestone in their clinical study XLRS. XLRS forms one of AGTC's five named ophthalmology development programs (XLRS, XLRP, achromatopsia and wet age-related macular degeneration). The XLRS clinical study involves the specially engineered technology licenced from the University of Florida which enables enhanced penetration to the back of the eye.

AGTC filed an application back in March to advance the trials onto a Phase I/II clinical trial expecting to enrol 27 patients at four locations with trials beginning by the end of 2015. This milestone announcement will earn AGTC a $5million from BioGen.

This announcement comes soon after AGTC and BioGen announced a partnership agreement, costing BioGen $124m after the waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976 expired and the satisfaction of other customary closing conditions. The two companies have combined to develop gene-based therapies focused around five retinal diseases, three of which are in early stage discovery.

CEO of AGTC, Sue Washer, has commented on this "encouraging time of growth for the Company" with them "looking forward to advancing this collaboration to accelerate the development and commercialisation of novel gene-based therapies".

- W Villiers

VOYAGER THERAPEUTICS' NEW APPOINTMENT TO B.O.D.

Gene therapy company Voyager Therapeutics, developer of life-changing treatments for incurable and incapacitating diseases of the central nervous system (CNS), has announced a new appointment to its board of directors. **Perry A Karsen** who is currently CEO of Celgene Cellular Therapeutics and has more than 30 years of experience in the biopharma industry.

LION BIOTECHNOLOGIES HIRE GREGORY MACMICHAEL, NOVARTIS

Lion Biotechnologies, Inc., a biotechnology company developing novel cancer immunotherapies based on TILs, has announced the appointment of **Gregory MacMichael** as Vice President of Process Development. Dr MacMichael has over 30 years' experience in drug product development and joins Lion from Novartis' Cell and Gene Therapies Therapeutic Unit, where he led process development for CAR-T and other immunotherapies.