

# Cell and Gene Therapy World



**Facilitate Cell & Gene  
Therapy World,  
Washington DC, USA  
26–27 January 2016**

On January 28, 2016, the National Oceanic and Atmospheric Administration announced that the January 22–24 snowstorm that hammered the US Eastern shoreline, was a Category 4 (or “Crippling”) on their Northeast Snowfall Impact Scale and that it was also the fourth largest to impact the northeast of the United States since 1950. Among the major metropolitan areas that were affected, the nation’s capital, Washington DC, was one of the hardest hit. The Facilitate Cell & Gene Therapy World 2016 event, which had been set to take place in DC on January 25–27, caught the aftermath of the storm on the chin and due to some extraordinary work by the event organizers, Washington DC city officials, and the numerous attendees who braved the weather, the event got underway.

### **Emily Culme-Seymour**

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## JUST HOW ROBUST IS THE CELL & GENE THERAPY SECTOR TODAY?



**Chair:** Stephen Potter (AGTC)

**Panelists:**

William Podd (Landmark Capital/Landmark Angels)

Vincent Ossipow (Omega Funds)

Josh Schimmer (Piper Jaffray & Co.)

### FINANCING

Day 1's session on financing featured a panel consisting of **William Podd** (Founder, President & CEO of Landmark Capital/Landmark Angels), **Dr Vincent Ossipow** (Venture Partner at Omega Funds) and **Dr Josh Schimmer** (Managing Director and Senior Research Analyst at Piper Jaffray & Co.) to define the prospects and resilience of the cell and gene therapy field in investors' eyes, as chaired by **Stephen Potter** (Chief Business Officer at AGTC). The panel kicked off with a discussion about the new trend in a universal method to targeting cancer, involving genomic approaches to allow more accurate predictions on what is going to happen to the individuals following treatment. The panel had a belief that this type of healthcare, once realized, would be paid for by the insurers and will ultimately improve patient care. It was suggested that the structure and approach to academic discovery has adapted in recent years to be more open to industrial development, and ultimately all agreed that the recent dramatic rise in momentum for the industry has been driven by impressive and material scientific progress.

Together with this rapid growth in exciting scientific discovery and clinical application, however, come interesting challenges in industrial

translation, such as dealing with the dynamics of competition. The panel were unsure whether there is an ultimate opportunity to have three separate gene therapy companies each targeting hemophilia as a sole indication, for example, but agreed that upon the demonstration of the new technology in one disease, other diseases are opened up as potential targets and the demonstration of viable platforms show scalability for companies in the long run. When questioned upon how to pick investment choices in these types of situations, the panel agreed that whilst there might currently be 'more contenders than winners', ultimately there is still a lot of scope for up-side investment returns if those winners are chosen.

Common frameworks for decision-making amongst the panel included analyzing the existing strategy for route to market, IP position, composition of the board and management team, as well as any existing ties with big pharma and biotech, with the latter demonstrating that an exit strategy is already in the line of site of the individual company. Some panel members believed mergers and acquisitions would mostly likely be the key activity going forwards in terms of funding coming in to the sector, but all ultimately agreed that the key message to convince potential investors on is the strength of the science that an individual company might be pursuing as well as what might differentiate and distinguish that company from a potential competitor. Whilst a number of unknowns still certainly exist in terms of exit routes for cell and gene therapies, such as drug pricing models, the panel were highly optimistic in the platform

and power of the science to successfully drive the industry forwards. Healthcare investors have been able to generate positive returns in recent years compared to previous activity and thus money is available, so with the scientific progress and driver for innovation existing in current academic groups and start-up companies, there are many reasons to be optimistic!

This discussion was followed by an interesting vision on trends in therapeutics from **Dr Gbola Amusa** (Director of Research and Head of Healthcare Research at Chardan Capital Markets LLC), who has a framework approach to assessing companies and individual assets in the field of cell and gene therapy. This is based on weighing what drives the products in development, in terms of the genetic phenotype being targeted and the clinical effects likely to be seen in particular patient subsets. After disappointing results seen in the Celladon heart failure and Avalanche Biotechnology wet age-related macular degeneration gene therapy trials in 2015, he believes it makes good sense for gene therapy companies to be focusing on monogenic diseases

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with a clear phenotype, especially those where small amounts of protein expression can make a positive clinical difference, and where delivery of that protein is technically feasible. Gene therapy has shown positive results in SMA, MPS-IIIb (San Fillipo B) and hemophilia B clinical studies, where predictions on cost savings on recombinant protein therapy are favorable towards gene therapy in terms of cost-benefit models. Conducting larger natural history studies to use as more accurate measures of potential benefit and cost-effectiveness would ultimately increase the applicability of these models.

## CELL THERAPY MANUFACTURING: DELIVERING COMMERCIAL SCALE-UP/SCALE-OUT STRATEGIES TO MINIMIZE CoGS



**Professor Chris Mason** (CSO, AVROBIO) chaired a session on manufacturing approaches to minimize cost of goods (CoGs) when looking at commercial scale-up or scale-out strategies. **Claudia Zylberberg** (CEO of Akron Biotech) first presented on some critical CoGs

drivers, such as grades of material available, cost issues, both in terms of the availability of single-use units and in meeting regulatory requirements, and also safety requirements, in terms of sterility, and the testing required within processes and in final formulation. With regards to

**Chair:** Chris Mason (AVROBIO)

**Speakers:**  
 Claudia Zyleberg (Akron Biotech)  
 Brian Hampson (PCT)  
 Ian Harris (J&J)

raw materials costs, the cell type and source in a large part dictates these, involving both facilities and personnel training, and the validation of cell yield, purity and functionality testing. Long-term supply agreements, following the coordination of pricing, volume predictions and supply requirements, can enable the control of pricing of raw materials in some instances.

**Brian Hampson** (VP of Manufacturing, Development & Engineering at PCT [Caladrius]) continued the discussion by outlining what he would define as patient-specific cell therapy and looking at what strategies are needed to achieve its successful routine delivery in the future. The challenges, such as single-patient batch sizings, mean that a failure of a production lot can unfortunately mean a failure to treat a patient, as well as life-threatening risks in delivering a production lot to the wrong patient. The key to achieving consistently high product quality and reasonable CoGs to meet demands over the commercial life of the product is, he argues, down to starting with a Quality Target Product Profile (QTTP) to develop the specific product characteristics, followed by the application of ‘development by design’. One essential risk to mitigate is the cost of idle capacity, which affects the total cost of goods per dose significantly, depending on the amount of doses able to be manufactured, and can be addressed by optimizing the distribution of production and sharing infrastructure. When questioned on the risk of failed lots, Brian suggested that the sooner one can be aware of a product lot failing the better, since early detection using in-product testing and subsequent termination mean that losses can be minimized, although

lot failure is still inevitable in some instances, hence CoGs models routinely allow for this. **Dr Ian Harris** (Product Development Team Leader for Cell Therapy at Janssen Pharmaceutical R&D) later added to the session with his experiences on automation, stating that whilst automation is expensive to realize and yet to be fully established for a number of cell therapy manufacturing platforms, the investment should be carefully thought through. An individual approach to automation should fit in with what one is wanting to achieve with the product i.e., less of a need to adapt to proof of concept studies, compared to where an actual product is being commercialized. However, even in the case of the former, a sensible strategy allowing for the products to adapt to automation as much as is feasible certainly ensures that no value is lost at the earliest stage.

“Whilst the risk of a particular asset diminishes along the stages of clinical development, so too does the tolerance to risk.”

In suggestions on how to start looking at automation, Ian proposes that first a process map or flow diagram of the specific manufacturing process can be built and then subsequently analysed to look for steps that can be reduced or eliminated, at the same time as increasing yields. In some cases, the final filling process is one that has not been sufficiently invested in, yet can be a good opportunity for increasing capacity, whilst ensuring that any limits in labeling and cryopreservation capabilities are then likewise addressed.

## CARS, TCRS, NK CELLS: ARE THE NEW WAVE OF CELLULAR CANCER IMMUNOTHERAPIES REALLY JUSTIFYING THE HYPE?



**Speaker: Adrian Bot (Kite Pharma)**

At a parallel CARs, TCRs and NK cells immunotherapy focus session, Dr. Adrian Bot (VP Translational Medicine, Kite Pharma) talked about B-cell aplasia, which is a common off-tumor on-target side effect of CD19-CAR T-cell therapy. He shared some interesting data on the recovery of B-cells in lymphoma and CLL patients. In Kite’s trials, data has shown that the CAR T-cells do not persist for a long time and

in fact are cleared 1-3 months after infusion. Despite the lack of CAR T-cell persistence, however, efficacy is durable. With clearance of the CAR T-cells, the company observed recovery of B-cells in more than half of the patients after a few months of infusion. Importantly, the recovery of B-cells is durable beyond one year in around 80% of the patients, with Adrian commenting that “B-cell aplasia is not obligatory”.

## CELL-BASED IMMUNOTHERAPY/ EX VIVO GENE THERAPY: MANUFACTURING BUSINESS MODELS FOR COMMERCIAL SUCCESS



**Chair: Isabelle Rivivere (Memorial Sloan Kettering)**

**Speakers:**

**Mark Dudley (Novartis)**

**David Sourdive (Cellestis)**

In the afternoon of Day 1, **Dr Isabelle Riviere** (Director, Cell Therapy & Cell Engineering Facility at Memorial Sloan Kettering Cancer Center) chaired a session looking at manufacturing business models for commercial success of cell-based immunotherapies and *ex vivo* gene

therapies. **Dr Mark Dudley** (Director, Cell Process & Development, Cell & Gene Therapies at Novartis) started by discussing the transfer of the CTL019 product candidate from the University of Pennsylvania (UPenn) facility in to Novartis, who are developing a pipeline of CAR-T

Design-based approaches can improve individual manufacturing steps in order to achieve an overall highly standardised process, whilst maintaining product safety and efficacy.

products and technologies in a collaborative agreement with UPenn. In the transfer of the manufacturing processes from the academic facility setting to large-scale manufacturing, the product and process characterization steps are continuing to evolve, due to different pressures both in terms of achieving delivery to satisfy global demand and addressing both financial and time-based constraints. In terms of how this was specifically achieved, the industrial manufacturing group had to watch the process at UPenn, map the individual stages and conduct risk assessments and data mining, and then start a series of test runs together with staff training. Subsequent comparability runs were conducted both within the industry setting and at the UPenn facility to crosscheck and validate successful transfer. Routine review of process capability is being carried out, as well as developments in expanding logistical routes and infrastructure, in order to deal with delivery of the patient-specific products and process scale-out. With a narrower process range existing within an industrial process compared to an academic process, different levels of quality are required for compliance adherence, which can mean a careful implementation of aspects such as reagent supply and closed-system

equipment. However, in taking apart the process and looking at unit operations, some systematic improvements can be made and innovative solutions considered, and particularly labor-intensive processes optimized to achieve cheaper, faster and easier production. Design-based approaches can improve individual manufacturing steps in order to achieve an overall highly standardized process, whilst maintaining product safety and efficacy. Overall, the technology transfer from the academic manufacturing setting to achieve an industrial process was successful, and comparability runs carried out in the industrial facility have minimized the variability in cell number in CAR T-cell culture observed in the academic setting.

Later in this session, **Dr David Sourdiv** (Executive VP, Corporate Development at Cellectis) presented on Cellectis' manufacturing platform using healthy donor material to produce gene-edited CAR-T products. Cellectis is focused on the use of a gene editing approach involving TALENs and part of the portfolio is focused on TALENs-engineered CAR-T cells, with existing alliances on a number of specific targets already defined with both Servier and Pfizer. The maturity of the technology in targeting precise gene sequences using TALENs editing means that this can be deployed in the CAR-T setting and allogeneic cells can thus be modified in order to suppress their capacity for alloreactivity, via the modification of endogenous TCR genes within the T cells themselves. Compared to the more common use of autologous T cells as therapies, this means an 'off-the-shelf' product can be achieved. The 18-day manufacturing process

involves the screening of healthy donors to derive defined and QC-controlled starting material followed by T-cell activation, lentiviral-transduction with CAR constructs, electroporation with TALENs and removal of residual TCR+ cells. The UCART19 product in development with Servier demonstrates the robustness of this process and Servier are moving forwards with the product, whilst Collectis have a number of other assets for various cancer targets using the TALENs gene editing approach already in preclinical development, including

CD123, CS1, CD38 and CD22. Longer-term data on the persistence of the cells *in vivo* will be important in demonstrating clinical efficacy, though ultimately cell survival *in vivo* for a large period of time might not be essential to the mechanism of action of targeting the tumour or at least enabling the tumour to be more visible to the existing immune system. David believes that gene editing demonstrates a differentiated approach to the use of T cell therapies to treat cancer, likely bringing additional value to treating a broad spectrum of indications.

## HOW MUST PAYERS & INDUSTRY ADAPT THEIR PRICING & REIMBURSEMENT MODELS TO NEW MARKET REALITIES?



Day 2 started with a morning plenary on pricing and reimbursement models, featuring a perspective based on current experience with a gene therapy product as presented by **Alec Orphanidis** (Senior VP, Global Commercial Operations at uniQure), followed by a panel composed of **Dr. Ed Pezalla** (VP & National Medical Director at Aetna), **Dr. Anirban Basu** (Stergachis Family Endowed Professor & Director, Pharmaceutical Outcomes Research & Policy Program at the University of Washington) and **Dr. Miguel Forte** (COO of TxCell SA). Alec first framed his thoughts on market access for gene therapy in the context of uniQure's product, Glybera, which is the first gene therapy product to have a marketing authorization within the EU. Glybera

is indicated for LPLD, an ultra-rare disease with a prevalence of only 1–2 per million, though the specific label means Glybera is a suitable treatment for around 30% of the LPLD population, resulting in around 500-1,000 treatable patients in the EU. uniQure first sought national reimbursement in Germany and incorporated 5-year data showing the resulting long-term benefit into their reimbursement paperwork. The company also sought an individual case request to the specific insurance company of an identified patient around the same time. Whilst the national reimbursement has not proceeded through yet, the individual patient case was successful and the patient was treated in Q3 2015, hence uniQure will be continuing with future patients as individual

**Chair:** Alec Orphanidis (uniQure)

**Panelists:**

Ed Pezalla (Aetna)

Anirban Basu (University of Washington)

Miguel Forte (TxCell SA)

requests along the same course. Given this experience, Alec advises that although research and development of orphan drugs has been incentivized via promising accelerated regulatory routes, there are issues with broadly applied incentives at the patient access level. Some countries do have specific health technology assessment methods or exemptions for orphan products, but the bulk do not, and orphan patient populations are small and heterogeneous in their nature, thus do not enable easy routes forward. It will be crucial to assess the new acceleration incentives carefully in order to understand when in the course of approval is the right time for patients to access the new treatments. Though a number of feasible reimbursement models have been proposed, challenges exist with each. For example, with an annuity payment model, if the patient leaves or stops responding then how does the overall payment programme adapt? In risk sharing models, would a higher price be paid if the patient continues to respond? Adaptive pricing would be another route capable of incorporating additional data at a later stage to affect the overall price paid, and a payment fund would allow companies to be paid immediately through a financial intermediary who can then recover their own costs (at a fee) at a later date, but the specific pathways of such approaches

are yet to be fully road-tested. Alec advises that the community needs to address these models quickly, in order to ensure patient access to the large number of novel therapeutics coming through the pipeline.

The panel followed this case study with similar perspectives on the need to manage access to care appropriately, thus ensuring that the intended patient subsets are the ones that get the benefits. Miguel stresses that defining targets and understanding the market with patient access in mind allows developers to position their products carefully and helps to mitigate risks against successful launch. The panel agreed that risk sharing approaches to reimbursement make the most sense when some levels of uncertainty exist, but that developers need to agree at the outset on the specific outcomes that are used to assess and measure the durability of the response, and at the same time be open to flexibility in the model at later stages. Increasing the development in health technology assessments and looking at how to manage these in complex disease settings will help address limitations in the models currently available, and at the same time characterizing disease progression over time for patient subsets will ensure patient benefit from new products in the long-run.

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## CAR T-CELL MANUFACTURE

**Speaker:** Tim Oldham  
(Cell Therapies Pty Ltd)

At the end of day 2, one of the highlights was a presentation by **Dr Tim Oldham** (CEO & Managing Director, Cell Therapies Pty Ltd) on the variability within apheresis collections for CAR T-cell manufacturing. Apheresis collection is the most critical and yet the most variable material in the whole autologous therapeutic product manufacturing exercise. Insufficient apheresis collection is an external risk factor that can ruin a defined manufacturing process and lead to production failure. The problem with apheresis is amplified in CAR T-cell multi-center trials where each collection facility may have hugely variable products. Tim suggests that the community looks to standardize apheresis collections to minimize the risks of manufacturing failure by developing uniform collection protocols and ensuring robust training of operators. However, donor (i.e., the patient in an autologous setting) variability cannot be avoided and is affected by a variety of factors, such as chemotherapy pre-treatments or prior stem cell transplants, as well as existing tumor burden, co-morbidities, and immune system status. Tim calls for community collaboration on the data captured from apheresis collection specifications and believes that such a database could be freely shared among the industry to benefit everyone developing cell and gene therapies.



## TECHNOLOGY CONVERGENCE: THE CONSOLIDATION OF KEY TECHNOLOGY AREAS IN CELL & GENE THERAPY

Day 2 also included analysis on big pharma activity in the cell and gene therapy space from **Dr. Jay P. Siegel** (Chief Biotechnology Officer & Head, Scientific Strategy & Policy at Johnson & Johnson) and **Dr. Devyn Smith** (Head of Strategy, Pharmatherapeutics Research & Development at Pfizer). Both speakers reflected on lessons learnt through collaborative approaches, in that relying on both internal and external expertise in cell and gene ensures overall success for both partners, since close communications with those who have experience in the new technologies allows the critical decisions to be made on when to or when not to partner. Devyn sees it as a highly positive step that nearly all big pharma is now involved in the cell and gene space, and moving from the old approach of building all capability internally, the importance of an external view and complementary approach to building expertise in the cell and gene sector has now been realised. Whilst the delivery of patient-specific products requires

a whole new business model for big pharma to adapt to, there is a lot of existing expertise capable of addressing these challenges and achieving a successful pivot to the new approach. Those with a willingness to see the potential in disruptive technologies and who have an openness for change will ultimately succeed.

The historical model of the development pipeline for new technologies going from academia to biotech to pharma has been superseded by direct routes from academia to pharma, realized by investments into new collaboration opportunities and coordinated approaches to translation.

Ultimately how pharma assess new potential opportunities remains the same: a combination of top quality science, a skilled management team, and an overall fit in terms of strategy and capability, followed up by long-term financial viability.

This year's Cell and Gene Therapy World featured the inaugural 1-Day Executive Briefing on Japan (with RepliCel's newly appointed President, CEO and Director, Lee Buckler scheduled to chair the event, but who was unfortunately unable to make it due to the adverse weather) chaired by the author, Colin Lee Novick. This section provides an overview of the key topics discussed over the course of the 1-day event.



## HOW WILL YOU CAPITALIZE ON JAPAN'S NOVEL COMMERCIAL, PARTNERING & REGULATORY OPPORTUNITIES FOR REGENERATIVE MEDICINE?

**Chair:** Colin Lee Novick  
(CJ PARTNERS)

**Speakers:**  
Akihiro Shimosaka (Asian Cellular Therapy Organization)  
Dr. Akihiko Iwai (FIRM)  
Mr. Tim Applebury (JETRO)

Clearly defining the specific nature of the opportunity presented by Japan's regulatory evolution **Dr Shimosaka** (Chairperson, Asian Cellular Therapy Organization), a long-standing authority on cellular therapy in Japan, provided the audience with an overview of the two Japanese laws that govern the regenerative medicine landscape of Japan: The Act on the Safety of Regenerative Medicine (ASRM) and The Pharmaceuticals and Medical Devices Act (PMD. Act). In providing this overview, his presentation touched upon the various reasons why these acts were put in place, such as the previously inadequate legal standing of the provision of certain cellular therapies that fell outside the scope of the PMD. Act (then known as the Pharmaceutical Affairs Law or PAL) and the fact that the previous approval framework did not adequately address the characteristics of cellular and gene therapies. A particularly helpful portion of the presentation, for those interested in Japan, was a list of some of the regulatory guidelines

that are available including the following:

- ▶ Guidelines on Ensuring Quality and Safety of Products Derived from Processed Human Cells/Tissues (2008)
- ▶ Guidelines on Ensuring Quality and Safety of Products Derived from Processed Human Stem Cells (2012)

**Dr Iwai** (Vice Chairman, FIRM and Divisional Senior Vice President, Astellas Pharma Inc.) provided a high-level overview of the Forum for Innovative Regenerative Medicine (FIRM), Japan's largest and most influential industry group within the regenerative medicine space. The presentation was largely centered on providing the listeners with an understanding of what sort of organization FIRM is. Of note was the rapidly expanding number of institutions that have signed agreements of some sort with FIRM over the past year; the Alliance for Regenerative Medicine (ARM), the Embassy of Sweden, the Center for Commercialization of Regenerative Medicine (CCRM), the Embassy of

Australia, and the UK BioIndustry Association. Those companies looking to enter Japan with their cellular/gene therapies will have no doubt also found the information on the newly established Regenerative Medicine Industrialization Task Force (RMIT) to be of particular interest.

Along with FIRM, the Japan External Trade Organization (JETRO) is another easily accessible resource when considering how to enter the Japanese regenerative medicine market. **Mr Applebury** (Business Development Representative, JETRO) provided listeners with an introduction to JETRO and a further look at the two laws governing regenerative medicine in Japan (the ASRM and the PMD. Act), but the most intriguing portion of his presentation was the announcement of the soon to be established Subsidy Program for Global Innovation Centers with a total subsidy of 1b JPY to be set aside for industries such as Regenerative Medicine

Looking to dispel some of the more prevalent misconceptions about Japan’s newly enacted regulatory framework, the author’s first presentation provided a deeper look into the ASRM and the PMD. Act. First off, the presentation noted that the “risk categories” that are so often mentioned when companies look to enter Japan, pertain strictly to the ASRM and if a company is looking to obtain reimbursement (which can only be obtained via the PMD. Act route) they are a moot point. Second, a closer look at what was meant by “probable efficacy” (a prerequisite for obtaining conditional approval under the new framework) was shared with the audience. Finally, a closer look at why TEMCELL® HS Inj. was given regular approval and HeartSheet was given conditional approval was discussed, with the difficulty of rigorous statistical analysis being the main driver for the decision.

## SHARING EXPERIENCES TO DATE OF WESTERN INDUSTRY TRAILBLAZERS SEEKING TO ACCESS THE JAPANESE REGENERATIVE MEDICINE MARKETPLACE

Pluristem is one of the few non-Japanese companies that is trying to tackle the Japanese market without teaming up with a firm that already has a domestic/Japanese presence. **Dr Kleinhaus** (Divisional Vice President, North America) provided the audience with some first hand experience of the process that her firm was been through in

their ongoing march towards obtaining conditional approval for their PLX-PAD therapy for Critical Limb Ischemia (CLI) in Japan. Dr Kleinhaus noted that Pluristem had already conducted a “Regenerative Medicine Manufacturing Quality/Safety Consultation” (on the manufacturing process) and a “Regenerative Medicine Consultation” (on



**Chair:** Colin Lee Novick (CJ PARTNERS)

**Speakers:** Karine Kleinhaus (Pluristem)

Michell Coffey (Mesoblast)

David Smith (Lonza)

the proposed clinical trial protocol) with the PMDA en route to a proposed CTN submission later this year. One of the most interesting portions of the presentation was the section that provided Pluristem's thoughts on how a company could demonstrate "probable efficacy."

Pluristem learned, through discussions with the PMDA, that the design of the study can meet the probable efficacy criteria in several ways, including through the use of surrogate endpoints rather than hard clinical endpoints. Products may still be eligible for conditional time-limited marketing authorization even if a primary endpoint of the trial is not met, based on outcomes of secondary endpoints that are considered "likely to predict efficacy"

As the only non-Japanese company with an approved regenerative medical product on the Japanese market (i.e. TEMCELL® HS Inj.), Mesoblast can provide others with valuable insights on the way forward in Japan. **Ms Coffey** (Senior Director Regulatory Affairs) provided her listeners with a number of these insights in her presentation, none of which was more pertinent than her opinion that existing information on what can (and what cannot) be considered for conditional approval is still rather vague (a position the author wholeheartedly agrees with). In her words "Serious unmet medical needs, orphan and those involving complex

surgical procedures seem to be best candidates" for the expedited route to market in Japan. Ms Coffey also noted an important point in that GMP manufacturing outside of Japan is permissible so long as said manufacturing meets Japan's quality standards.

Lonza's **Mr Smith** (VP, Global Business Development) provided a different angle for companies to consider when entering the Japanese regenerative medicine market. Namely, that of partnership. His presentation explained at length the process that went in to determining Nikon as the firm's Japan partner, such as ensuring that the "cultural fit," "expertise and knowledge," "business goals," and "financials" were aligned between the partners. He further highlighted an extremely important point when one is looking to strike up a partnership with a more traditional Japanese company when he noted that "Everything takes longer than expected, start early, set realistic timelines, build contingencies, calmly work through issues." Finally, he presented some long-awaited information about the proposed NIKON CeLL innovation manufacturing facility such as its location (near Shiomi Stn. Tokyo), expected service provision commencement (Autumn 2017), and total floor area (6,000 m<sup>2</sup> across two floors) making it one of the largest regenerative medicine CMOs on the Japanese market.

"Everything takes longer than expected, start early, set realistic timelines, build contingencies, calmly work through issues." David Smith, Lonza, USA

## PROFILING THE OUTSOURCING, INVESTMENT, PRICING & REIMBURSEMENT ENVIRONMENTS IN JAPAN FOR CELL & GENE THERAPY



In addition to being a prominent member of the FIRM organization, **Mr Suzuki** (Vice Chairman & Member of the Board, MEDINET, and Vice Chairman, FIRM) is a long-standing advocate for regenerative medicine in Japan through his involvement with MEDINET. His presentation focused on providing a high-level overview of the new laws (i.e. the ASRM and the PMD. Act) but with a focus on the National Health Insurance (NHI) pricing structure that was implemented on the recently approved regenerative medicine products (i.e. the average price for a standard treatment):

- ▶ **TEMCELL® HS Inj.** (JCR Pharmaceuticals): 13,989,800 JPY
- ▶ **HeartSheet** (Terumo Corporation): 14,760,000 JPY

His presentation concluded with an introduction to MEDINET's newly completed 2,990.5m<sup>2</sup> manufacturing facility, located 10 minutes from Haneda (Tokyo International) Airport. He highlighted that the facility provides solutions both for products developed under the ASRM (i.e. specified cell products) and those developed under the PMD. Act (i.e. regenerative medicine products)

The author's second presentation of the day focused on the NHI pricing methodologies that are in place for regenerative medicine products in Japan and a closer look at the various players that are operating within the regenerative medicine

products market. Unlike the PMD. Act, which created a new category for regenerative medicine products (alongside pharmaceuticals and medical devices), the Ministry of Health Labour and Welfare's (MHLW) Central Social Insurance Medical Council has not created a corresponding pricing scheme for the category. As such, the author stressed that all approved regenerative medicine products will be priced as either a "pharmaceutical" or a "medical device." Specific examples (i.e. TEMCELL® HS Inj. and HeartSheet) of how these NHI prices were determined were also provided. The author proceeded to provide the audience with an overview of the various market participants (CMOs/CPCs, CROs, SMOs, Pharmaceutical Companies, Distribution Companies, etc.), PMDA consultation statistics, a detailed look at the numbers of regenerative medicine product R&D being conducted in Japan (including therapeutic categories), and specific examples of foreign biotech's and Japanese pharmaceutical company's recent developments in the field.

Prof. Mason (COO AVROBIO), concluded the session with an open discussion on how pharmaceutical companies could potentially utilize the Japanese regenerative medicine regulatory framework as part of a new R&D strategy. Namely, instead of seeing the Japanese market as one to deal with after having won approval in the US and Europe, to see

**Chair:** Colin Lee Novick (CJ PARTNERS)

**Speakers:**  
Kunihiko Suzuki (MEDINET)  
Chris Mason (AVROBIO)

it as the first market to tackle. He stressed that the newly implemented conditional approval framework in Japan allows companies (especially biotechs) with a valuable alternative source of capital to further their R&D in jurisdictions outside

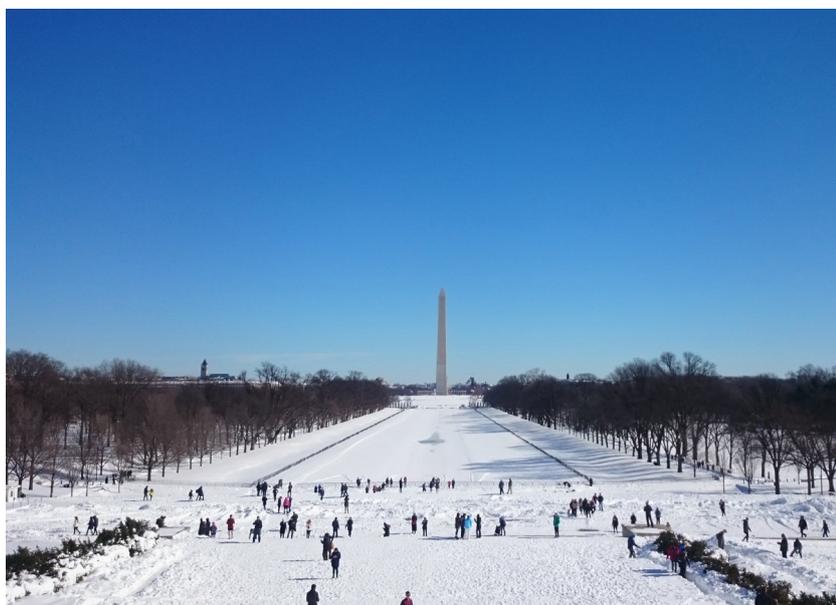
of Japan. He added that the developments in Europe bode well for further development, post obtaining approval in Japan, in the jurisdiction with the US following close on the heels.

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## CONCLUSION

As the 1-Day Executive Briefing on Japan was originally scheduled to take place on January 25, changing the date to Jan 26, resulted in some unfortunate double bookings of presentations at the event. Coupled with the fact that a good number of participants were unable to attend the event due to the snowstorm, this meant that the overall attendance at the briefing was not ideal. However, for those who were able to make it, the briefing provided a rare in-depth look at the exciting Japanese

regenerative medicine market, with a plethora of information in English that was heretofore only available in Japanese. Moving ahead, the author for one looks forward to more iterations of the briefing at subsequent Phacilitate events. As the PMDA slowly solidifies the various aspects of the new framework, there will be ample opportunity to scrutinize the ramifications and figure out how best to utilize the now, in the case of regenerative medicine, much more open Japanese market.



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