

Commercial Considerations For Cell And Gene Therapies: Viewpoints From The 2016 ARM Meeting

The Alliance for Regenerative Medicine held its annual *Cell & Gene Meeting on the Mesa* in La Jolla, CA, in early October. Over the course of the three-day partnering meeting and scientific symposium, several important issues affecting the cell and gene therapy industries were discussed, including commercial considerations.

From a regulatory standpoint, the cell and gene therapy field is growing rapidly. Celia Witten, MD, PhD, the deputy director of the FDA's Center for Biologics Evaluation and Research, reported that there has been an explosion of investigational new drug (IND) applications submitted to the Office of Cellular, Tissue and Gene Therapies (OCTGT) over the last couple of years, including over 200 submissions in both 2014 and 2015. Furthermore, the dealmaking climate for cell and gene therapies has encouraged investment and more innovation. With several cell therapies on the market, and a few gene therapies that have now been launched in Europe and the US during recent years, the field can now benefit from past experiences in commercialization and lessons learned. A panel of biopharma executives met on day 2 of the ARM meeting to discuss aspects of commercialization that are unique to the gene therapy sector.

"Commercialization is more than just pricing." This quote, from the president and chief executive officer of **Applied Genetic Technologies Corp.** Sue Washer, represents the overarching theme of the commercial panel discussion. Washer acknowledged that, understandably, cell and gene therapy drug developers want to see a return after working on the development of a product for years. However, the real focus should be on the patient and the societal benefit. She said it is important that through the clinical development plan, the company gets the data it needs for not only regulatory approval but also for other stakeholders to show value to the patient and society. Sven Kili, MD, vice president and head of cell and gene therapy development at **GlaxoSmithKline PLC**, agreed that creating value for patients, parents and stakeholders should be at the forefront; what a company charges and gets reimbursement for comes at the end.

In a discussion on value challenges, the panelists pointed out that cell and gene

therapy is a unique case study. Elizabeth White, PhD, the assistant vice president for early commercial planning in rare disease and gene therapy at **Pfizer Inc.'s Pfizer Innovative Health**, said that these therapies are designed to last for a long time, but the ability to show that in clinical trials is limited. GlaxoSmithKline's Kili further backed up that point, admitting that the field is uncharted territory. Companies just do not know yet what will happen to patients receiving cell or gene therapy 30,

payers may not have much or any experience. She gave the example of rare blinding diseases, in which her company is involved, saying that payers are not yet experienced with reimbursing for any products that cure blindness. Therefore, it is the developer's job to produce the primary data on health economics and to do that early.

GlaxoSmithKline's *Strimvelis* was the most recent cell and gene therapy to be approved worldwide. The European Commission granted marketing authorization on May 27, 2016 for the *ex vivo* stem cell gene therapy in severe combined immunodeficiency due to adenosine deaminase

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60 or 90 years down the road, for example.

The panelists discussed what needs to be done early on in development to demonstrate the value of cell and gene therapies. Matthew Patterson, president and chief executive officer of **Audentes Therapeutics Inc.**, stressed the importance of building in a collection of data that are robust enough to satisfy regulatory authorities and payers. For the latter group, it is equally important to add in quality-of-life measurements. He also said that early dialogue with external stakeholders, such as patient organizations, key opinion leaders and payers, would help. On the topic of interacting with payers early on in development, Applied Genetic Technologies' Washer pointed out that this is especially critical for those working in rare diseases where

deficiency, a rare disease affecting the immune system. GSK's Kili provided insight behind the company's strategy with *Strimvelis*. He said GlaxoSmithKline will not make a profit on this first indication for the drug (the company exercised options from its licensors **Fondazione Telethon's Fondazione San Raffaele del Monte Tabor and San Raffaele Telethon Institute for Gene Therapy** to also develop programs in metachromatic leukodystrophy and Wiskott-Aldrich syndrome). *Strimvelis* is expected to cost \$665,000, and Kili says the price is appropriate, not ridiculous (Kili also cited GlaxoSmithKline's pledge not to price a drug more than 14% of the R&D costs). In working with the Italian Medicines Agency (*Strimvelis* may only be administered in one clinic in Milan), GSK has committed to a money-back guaran-

tee, agreeing to refund the cost if the drug does not work. In terms of not making a profit initially on Strimvelis, the company has stated that its goal with the launch is to help patients and get experience with cell and gene therapies.

In marketing a cell-based gene therapy, Kili stressed GlaxoSmithKline's various responsibilities to its patients. He said it is critical to find ways to follow up with patients, and that GSK is committed to doing this for at least 15 years. Kili also mentioned the importance of logistics in *ex vivo* therapy, saying companies in this area need to put together logistical pathways so that the sponsor is always in control of and responsible for those cells on behalf of the clinicians and patients. He believes there needs to be complete comfort with who is handling the cells throughout the entire process. For Strimvelis specifically, with a limited half-life of the transduced cells, Kili said the logistics of patients having to travel to Milan for therapy is a key consideration for GlaxoSmithKline. The company is trying to make the drug available for patients closer to home, and is looking for hubs where more patients can be treated.

The introduction of cell and gene therapy into disease management has the potential to disrupt the clinical care pathway. Pfizer's White talked about this in terms of hemophilia, which is an area where her company is developing therapies through a deal with **Spark Therapeutics Inc.** There are already effective agents available for hemophilia. For example, severe patients are stable on prophylactic coagulation fac-

tor therapy on a regular basis, and payers have certainty around how much they are paying for these drugs. When cell and gene therapies come into the mix, they are expected to alter the care pathway, especially if they provide a one-time treatment for patients, meaning clinicians would no longer need to manage their disease. White stressed that there will be a need to follow patients over time to build the evidence base. Andrea Hunt, the vice president of new product therapeutic area lead gene therapy for neuroscience and ophthalmology at **Shire PLC**, agreed that the care pathway will change, but not all clinicians will adopt cell and gene therapy. In the hemophilia example, she said some patients will still need to take factor therapies, and that the old and new models will have to co-exist. This will further complicate value demonstration to payers, given the uncertainty around future factor consumption for patients who have received gene therapy.

Educating various stakeholders on cell and gene therapy was a key consideration of the commercial panel. Shire's Hunt, in talking about the disruption to the clinical care pathway, said that clinicians will require education for adoption of these therapies. Clinicians will also need education to ensure the products are applied appropriately, so that patients will get good results, and the patients themselves will have to understand the therapy and its shortcomings. GlaxoSmithKline's Kili pointed out that patients will get nervous, based on the fact that what is happening could be a permanent change to their

genome. Education is also important for outreach to parents of pediatric patients on cell and gene therapy. Kili told the story of a father who would not allow his dying child to take gene therapy out of fear, based on headlines in the media about gene therapy causing cancer. Examples like this, said Kili, are why parents need to be educated too, since they are in control of their child's health.

In a discussion on the unique capabilities required to bring a cell or gene therapy to market, the consensus was that manufacturing is critical. Audentes' Patterson, whose company is investing in manufacturing to build out its own capabilities, said that because manufacturing in this field is still in its infancy, and the science is complex, it is difficult to manufacture at a large scale. Applied Genetic Technologies' Washer agreed that manufacturing is an important consideration, adding that analytics will be critical too, stressing that regulatory agencies care about the robustness of the data and characterization standards. ▶

IV004948

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Editor's note: This article is excerpted from Alliance for Regenerative Medicine Conference, October 2016: White Paper, published in October 2016 by Informa's Datamonitor Healthcare, discussing some of the key highlights from various panel discussions on cell-based immuno-oncology, gene editing, pricing and reimbursement, financing and commercialization.



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