MDA Holds Summit to Address Challenges In Gene Therapy

MDA has invested over $125M in the development of gene therapy for neuromuscular diseases (NMDs) over the past 20 years. To continue to lead the way in this important field of medicine, MDA held a summit to address the challenges of AAV-based gene replacement therapy in NMDs. Organized by MDA's Chief Scientific Officer (Sharon Hesterlee) and VP of Research (Angela Lek), the meeting was held in Tucson, Arizona on January 26-27th, and included representative stakeholders from academia, clinic, industry and disease-specific foundations. The meeting itself was chaired by two leaders of the gene therapy field, Dr Carsten Bonnemann (NIH) and Dr Barry Byrne (Uni. of Florida). This meeting represented the first time top experts and stakeholders in gene therapy have convened to talk openly about adverse events linked to clinical trials in the field.

Experts agree that although gene therapy holds great promise in addressing the underlying cause of many neuromuscular diseases, treatment of human patients must overcome many challenges and risks. According to Dr. Bonnemann: "We have entered a very exciting era of tremendous hope and promise and already resounding successes. However, we are also entering an era where the challenges of gene therapy are becoming more clear with every patient that we dose. But in my view, these are challenges can be addressed as long as we understand them, understand the mechanisms and find solutions for them. The major challenges are around dose-related toxicities, immunology, durability, and efficacy."

The agenda also included a listening session led by Larry Miao, Rich Horgan, Chris and Jessica Curran, who all spoke on behalf of family members with neuromuscular disease. Their personal experiences provided a unique perspective on their expectations and concerns surrounding gene therapy. Dr Byrne recounts: "We had three families participating in the conference today. Despite the deep science that was discussed over the course of the day, I personally felt their contribution and certainly the investigators that care for those families, was really the highlight of the meeting. We have to be patient-focused. We have to be sure that safety is paramount and that families remind us of that all the time."

Specific topics discussed during the meeting include natural immunity to AAV in the patient population, re-dosing opportunities, capsid and transgene-related toxicity, persistence of transgene expression, immune responses, as well as general ethical considerations of gene therapy. The outcome of these discussions highlighted key areas for further study and provided critical impetus for more sharing of

information among the investigators and companies developing treatments for all diseases targeted by MDA. A white paper summarizing key outcomes from this landmark gathering is forthcoming. An additional goal of the meeting was to also identify potential funding opportunities for MDA to help in the safe translation of gene therapies across NMDs. MDA is anticipated to release grant funding opportunities to address specific issues pertaining to the safe translation of gene therapies identified during the meeting.

As a result of the positive feedback received from this meeting, the MDA will consider planning additional small-group meetings with strong focus on specific topics to encourage productive discussions between field experts and the community.

Dr. Alan Beggs (Boston Children's Hospital)

"The Summit was a unique chance to bring together key stakeholders, including MDA-funded academic neuromuscular researchers, biotechnology and pharmaceutical company sponsors of gene therapy clinical trials, the physician scientists treating their patients in these trials, and members of the patient community whose loved ones had received some of the first gene therapy treatments, providing a comprehensive overview of the promise, was well as the challenges we face developing safe and effective gene therapies for neuromuscular diseases."

Dr. Barry Byrne (University of Florida)

"Clinical trials have yielded such promising results that certainly the patient community and the scientific community are very positive about the prospect of a successful gene therapy in the neuromuscular space. So it's quite an exciting time, but yet there are challenges that we face as a community. We learned that today in the conference that was organized by the MDA to understand what challenges still exist in the gene therapy, the use of gene therapy in neuromuscular disease."

Dr. Carsten Bonnemann (National Institutes of Health)

"MDA has amongst the longest histories in the development of gene therapies for neuromuscular disorders and has always been instigating new developments to advance the field with funding opportunities for projects and investigators. This conference shows that MDA continues to strive to anticipate challenges, seeking to understand where to best put resources and issue requests for applications to help steer the field into the right direction. And I think that's a great idea."

Dr. Tahseen Mozaffar (University of California Irvine):

"Being involved in gene therapy trials in adult patients with rare and ultra rare myopathies, I found this summit really helpful. Learned a lot about current understanding of some of the complications and the underlying pathology behind these complications, such as systemic inflammatory responses and TMA. The relationship to vector dosing as well autoimmunity to the transgene, and how it contributes to these complications, was also helpful. I hope MDA will continue this series."