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January 26, 2018

Dear Pompe Patient Community Leaders,

At Audentes Therapeutics, we are focused on developing and commercializing gene therapy products for patients living with serious, life-threatening rare diseases. As with many rare conditions, there is limited published information available about the humanistic impact, or burden, that the condition has on the individuals and families living with it every day. While there is published literature discussing the clinical and humanistic burden of Pompe disease, there are still gaps in fully understanding certain aspects of the humanistic burden, particularly for infantile-onset Pompe disease (IOPD).

We believe that understanding the perspective of those living with Pompe disease and how it affects them is important to developing our clinical plans for new therapies to treat Pompe disease. Therefore, we recently partnered with medical experts to conduct and publish a comprehensive review, entitled, "The Humanistic Burden of Pompe Disease: Are There Still Unmet Needs? A Systematic Review." This article was published in the journal called *BMC Neurology* and can be found here, or at this link online: https://bmcneurol.biomedcentral.com/articles/10.1186/s12883-017-0983-2

This article discusses the significant humanistic burden associated with late-onset Pompe disease (LOPD), and highlights the lack of published information on this aspect of infantile-onset Pompe disease (IOPD). Humanistic burden is generally defined as the impact a condition has on an affected person or caregiver's overall health, quality of life, ability to undertake daily activities and other aspects that affect people's day-to-day lives. This is described as including quality of life, activities of daily living, caregiver burden, psychosocial and emotional issues, treatment satisfaction, adherence to treatment, pain, fatigue and sleep quality.

The article is a comprehensive review of 17 published medical articles containing information on the humanistic burden of Pompe disease, and concludes that individuals living with LOPD have a significantly lower Health-Related Quality of Life (HRQoL) than the general population. These individuals also have increased fatigue, reduced sleep quality, and increased pain and functional disability. Importantly, while enzyme replacement therapy (ERT) clearly has benefits for those living with Pompe disease, the literature suggests it may not significantly improve HRQoL measures.

In particular, the impact of pain and sleep quality appears to have generally been underestimated for Pompe disease. Ongoing pain is shown to relate to higher levels of anxiety and depression, and to interfere with daily activities, such as walking, ability to work, as well as mood, sleep and enjoyment of life. The data indicate that ERT may temporarily stabilize bodily pain, however, it may not reverse it.

The review also highlights the significant caregiver burden associated with Pompe disease. A single study of people with LOPD receiving ERT found that caregivers provide an average of approximately 18 hours per week of informal care, and that significant numbers of caregivers report mental and physical health problems, and financial and relationship stress.

This article also highlighted notable gaps in our understanding of Pompe disease. To date, there are no peer reviewed publications exploring the humanistic burden in IOPD, the most deeply affected patient population, and only one study evaluated caregiver burden in LOPD. Part of the value of these types of published articles is that they can help identify areas of unmet need to guide future research and development efforts for novel therapies for Pompe disease.

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What are leaders in the Pompe disease patient community saying?

David Hamlin of the United Pompe Foundation stated, "While Enzyme Replacement Therapy has made a noticeable difference in the lives of many Pompe patients, there are still many areas in which improvement is needed. This article takes an in-depth look at some of these areas and the overall role that they play in the well-being of not only the patient themselves but also the impact upon the family as a whole."

"This publication is a comprehensive summary of the many challenges experienced by Pompe disease patients, families and caregivers," stated Maryze Schoneveld van der Linde, Communications Coordinator of the International Pompe Association. "This systematic and comprehensive literature review serves as an important resource for innovative companies such as Audentes that are committed to incorporating patient focused outcome measures into their drug development efforts."

Allan Muir of AGSD-UK said of the publication, "Our charity works closely with Pompe patients to understand and support their non-medical needs; so, we fully understand the issues raised in this paper. We welcome its publication which we believe will lead to the acknowledgement of under-reported characteristics of Pompe disease and will assist with the development, regulatory approval and reimbursement of future therapies to reduce the disease burden."

"This publication does a very good job of bringing the burden of Pompe disease to the forefront. The results are consistent with what I've seen in our member population and on social media. I appreciate that this focuses more on the actual burden of Pompe disease on families and not just on test results," stated by Brad Crittenden, President, Canadian Association of Pompe.

Tiffany House, President of AMDA and Chairman/President of the International Pompe Association stated, "It is always promising to see new publications on Pompe disease. This especially true of publications that look at the broad effect that Pompe can have on the patient and their families. The patient community understands the effects of the humanistic burden of Pompe, and it is encouraging to see publications that begin to try to put this effect into quantifiable terms. I look forward to more research being done in this area, and I know the patient community will be eager to participate in it."

We hope you find this information to be useful and informative. We look forward to continuing to share information about Pompe disease as it becomes available. If you would like to reach someone at Audentes, you may contact Patient Advocacy at patientadvocacy@audentestx.com.

Sincerely,

Suyash Prasad MD, Pediatrician, Senior Vice President and Chief Medical Officer