[For potential posting on August 2, 2016]

On August 1, 2016 Biogen and Ionis Pharmaceuticals announced that nusinersen, our investigational treatment for Spinal Muscular Atrophy (SMA), met the primary endpoint pre-specified for the interim analysis of ENDEAR, the Phase 3 clinical trial evaluating nusinersen in infantile-onset (consistent with Type 1) SMA.

We recognize this exciting program milestone may bring certain questions to mind. Below we hope you'll find answers to some of these questions. If you need additional information, please feel free to contact Biogen's Patient Center at patientcenter@biogen.com.

1. **What is the ENDEAR study?**
   The ENDEAR study was originally designed to be a 13-month clinical trial including approximately 110 patients with infantile-onset (consistent with Type 1) SMA. The purpose of the trial was to collect well-controlled data for regulators to assess the safety and efficacy of nusinersen in this patient population. Initially, the study was designed with a primary endpoint of ventilation-free survival. As we gained more insight from our open-label studies, it became increasingly clear that measuring motor milestones could be a useful indicator of nusinersen's potential efficacy in the ENDEAR study. As such, the primary and secondary endpoints were updated in May of 2016.

2. **Why did you conduct an interim analysis? What does this mean?**
   When designing the ENDEAR study, we consulted extensively with regulators, experts in field and members of the community to design a protocol that would allow us to collect the necessary well-controlled data in the shortest time possible.

   We designed the ENDEAR protocol to include an option for an interim analysis prior to the formal conclusion of the trial in order to evaluate if a significant treatment effect was detectable ahead of the full data collection. The interim analysis has showed that infants taking nusinersen experienced a statistically significant improvement in the achievement of motor milestones compared to those who did not receive treatment.

   Because of the positive results of the interim analysis in the infantile-onset (consistent with Type 1) SMA population, all ENDEAR and EMBRACE study participants can elect to receive nusinersen by enrolling in the extension studies.

3. **What happens next?**
   We will continue to collect data on all of the participants enrolled in the clinical trial through their next office visit as we work to submit our regulatory filings. The regulatory filings will include the ENDEAR interim analysis data and all other clinical and preclinical data currently available. We anticipate we will be able to submit our marketing applications to both the FDA and the EMA in the coming months, with filings in other countries to follow. We are exploring expedited review options with both agencies and do not yet have a specific timeline for review and potential approval of nusinersen in either region. Review and approval varies by country, but, in general once accepted or validated, standard review in the U.S. is 10 months and review time averages between 13-15 months in the EU.

4. **What are your plans for the CHERISH study? Will you conduct an interim analysis with this trial, too?**
   Based on our ongoing conversations with regulators, data from a well-controlled study in later-onset (consistent with Type 2) SMA will be needed in order for them to assess the safety and efficacy of nusinersen in this population. Once we are able to collect enough well-controlled data to have a pathway to approval in that population, and we are able to end the CHERISH sham-controlled study arm, we will be able to make a determination about how to proceed.

   We are working to complete our CHERISH studies as quickly as possible and continue to explore all opportunities to shorten the timeline to review and potential approval.

5. **Are you opening an Expanded Access Program (EAP)?**
   Given the positive data from the interim analysis, Biogen is working to open an expanded access program (EAP) for eligible patients with infantile-onset SMA (consistent with Type 1). We hope this program will mark the initial phase in our effort to enable expanded access to nusinersen for patients with SMA.

   Existing clinical trial sites, because of their experience in administering nusinersen, can participate in the EAP in countries where EAPs are permitted according to local laws and regulations, can be operationalized and there is a path that can support long-term availability of nusinersen. Once the EAP is open and required local approvals are in place, individual participating sites may start enrollment after they have transitioned ENDEAR study participants to the open-label extension study.

6. **How can I find out if I am or my child is eligible for the EAP?**
   Please consult your physician to obtain the most up-to-date information on eligibility for the program.

7. **How will we find out more information about what's happening next?**
   The interim analysis represents an important milestone for the program, but we still have work to do as we move towards our number one goal of advancing nusinersen toward approval. We are committed to open and transparent communications with the SMA community whenever possible and will continue to update the community as the program progresses.

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