Dear Members of the SMA Community,

Today marks an important day in our collective pursuit of a meaningful treatment for Spinal Muscular Atrophy (SMA). We are pleased to share the exciting news that we have reported positive results from a pre-specified interim analysis of the ENDEAR study in infants with infantile-onset Spinal Muscular Atrophy (consistent with Type 1). As a result, plans are underway to transition all ENDEAR study participants to nusinersen in an open-label extension study and close the ENDEAR study. We plan to submit regulatory filings globally in the coming months. This step will hopefully bring us closer to our ultimate goal of making nusinersen available as quickly as possible as an approved therapy.

We would not be here without the support of the families participating in our clinical studies, the study doctors who provide exceptional care for these families, and the entire SMA community, who inspire us to be at our best each and every day. Thank you for your contributions which have brought us to this meaningful moment.

As we look to the future we want to share additional perspective on where we are today and where we are headed in the coming months:

- Based on the severity of the disease and urgent need in SMA, we designed the ENDEAR protocol to include an option for an interim analysis prior to the formal conclusion of the trial.
- We conducted detailed scientific analyses using all of the available data to identify the earliest point in the study when the interim analysis could be conducted to provide regulators with the well-controlled data needed to assess the safety and efficacy of nusinersen.
- 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 transitioning to the extension studies.
- Biogen is working to open an expanded access program (EAP) in the Autumn to make nusinersen available for eligible patients with infantile-onset SMA (consistent with Type 1) based on the unmet medical need in SMA and positive ENDEAR interim results.

Over the coming months we will work to submit our marketing applications to regulatory authorities in the U.S. and EU, with additional countries to follow. The marketing applications will include the ENDEAR interim analysis and all other clinical and preclinical data currently available. We are continuing to explore expedited review options with regulatory agencies, but we do not have specific timelines for review and potential approval. Regulatory review varies by country; in general standard review in the U.S. is 10 months once a new drug application is accepted, and review time averages between 13-15 months in the EU. This amount of time can vary greatly and can impact the timing to product availability. We will continue our additional studies in the nusinersen program, including CHERISH (later-onset consistent with Type 2), NURTURE (pre-symptomatic infants), and the ongoing Phase 2 open label studies (CS3a and CS12), in order to continue to collect the data to demonstrate the safety and efficacy of nusinersen in these populations.

In light of these regulatory review timelines, Biogen is working to open an expanded access program (EAP) in the Autumn of 2016, which will provide access to patients with infantile onset SMA (consistent with Type 1) prior to potential regulatory approval.

- 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 and can be operationalized, and where 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.
- Eligibility criteria and additional details on the infantile-onset (consistent with Type 1) EAP will be posted on clinicaltrials.gov in the coming weeks. This site will be the best place for you and your physician to obtain the most up to date information on the program.

We understand this EAP will not meet the needs of the entire SMA community. We intend to open an EAP in the later-onset (consistent with Type 2) population in the future, if and when we have collected enough positive well-controlled data to enable regulators to assess the safety and efficacy of nusinersen in this population and we are able to close the CHERISH sham-controlled study. We are working to complete our CHERISH study as quickly as possible and continue to explore all opportunities to shorten the timeline to review and potential approval.

Our respect and admiration for the SMA community's tireless efforts to advance SMA research and development for an approved treatment grows each and every day. We still have work to do, but this milestone advances us to the next steps in this endeavor. We will continue to share information and program updates to the community when possible and would like to express our deepest appreciation to all involved in this important journey.

Biogen and Ionis Pharmaceuticals