January 8, 2021

Dear SMA Community,

In response to your request, we are pleased to share with you an update on the RESPOND trial; a Phase 4 open-label, multicenter, single-arm study to evaluate the efficacy and safety of nusinersen in patients with a suboptimal clinical response to gene therapy (onasemnogene abeparvovec).

On January 8 2021, it was announced that the first patient has been treated in the global RESPOND study. The study will examine the clinical benefit and safety of nusinersen in infants and children with spinal muscular atrophy who still have unmet clinical needs following treatment with onasemnogene abeparvovec. In light of clinical and real-world experience reporting that patients previously treated with gene therapy have been treated with nusinersen, the study will seek to understand if the continuous production of SMN protein generated by nusinersen provides further clinical benefit to these patients.[1,2,3,4]

RESPOND Trial Overview
The study is projected to enrol 60 participants up to age 3 who are determined by the investigator to have the potential for additional clinical improvement after receiving the gene therapy (onasemnogene abeparvovec).

The primary study group aims to include 40 infants aged 9 months or younger (at the time of first nusinersen dose) who have two copies of *SMN2* (likely to develop SMA Type 1) and received gene therapy (onasemnogene abeparvovec) at 6 months old or younger. A second study group will include 20 children and will generate data in patients with a broader age range (up to age 3 at the time of first nusinersen dose). After a screening period, participants will receive the approved 12 mg dose of nusinersen administered IT by LP on Days 1, 15, 29, and 64 (loading doses), followed by a maintenance period during which the participants will receive 12 mg nusinersen IT every 4 months for two years.[5]

RESPOND is a phase 4, open-label study, so both the patient's caregiver and their physician are aware that they are being treated with nusinersen. The study will be conducted at approximately 20 sites worldwide.

Working in partnership
The SMA community has been instrumental in shaping the design of this study to ensure that the clinical outcome measures being used are those that matter most to patients, and we are grateful to all the families, caregivers and investigators who continue to help us improve care for families affected by SMA.

As a team we remain a dedicated, committed partner to this community and will continue to be available to provide updates in the future, when requested.

Best Regards,

Michaela Hrdlickova

Director Patient Advocacy SMA, Europe/Canada/Partner Markets, Biogen

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1 Zolgensma EU Summary of Product Characteristics (SmPC). Available at: https://www.ema.europa.eu/en/documents/product-information/zolgensma-epar-product-information_en.pdf. Accessed on Oct. 12, 2020.

2 Finkel R, et al. Presented at the Muscular Dystrophy Association's (MDA) 2020 Clinical & Scientific Conference.

3 Harada Y, et al. Presented at the Muscular Dystrophy Association's (MDA) 2020 Clinical & Scientific Conference.

4 Finkel R, et al. Presented at the World Muscle Society (WMS) 2020 Virtual Congress.

5. SPINRAZA U.S. Prescribing Information. Available at: https://www.spinraza.com/content/dam/commercial/specialty/spinraza/caregiver/en_us/pdf/spinrazaprescribing-information.pdf. Accessed on July 13, 2020