IONIS® InBrief
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SPINRAZA® highlighted in multiple presentations at World Muscle Society Virtual Conference

ASCEND study to evaluate a higher dose of Ionis-discovered nusinersen in SMA patients who had less than optimal response to Evrysdi

Ionis' partner Biogen recently announced plans to initiate ASCEND, a global Phase 3b clinical study designed to evaluate the clinical outcomes and assess the safety of a higher dose of nusinersen in children, teens and adults with later-onset spinal muscular atrophy (SMA) following treatment with Evrysdi® (risdiplam). Clinical data suggest that in some patients treated with Evrysdi, lower drug exposure may contribute to less-than-optimal treatment outcomes. Evrysdi's dosing is capped at 5-mg once patients reach a body weight of 20 kilograms. Available data indicates that exposure to Evrysdi diminishes with increased age and weight, with an approximately 40 percent reduction in drug concentration compared to infants.

People with SMA do not produce sufficient survival motor neuron protein, which is vital for the maintenance of neurons that support sitting, standing and movement. At the approved 12-mg dose, motor neuron exposure to nusinersen remains similar as patients age and grow.

Biogen markets nusinersen as SPINRAZA®, the first approved therapy for SMA that remains a global standard of care for treatment of the disease. To date, more than 11,000 SMA patients have been treated with SPINRAZA worldwide.

"Even though SMA patients now have multiple treatment options, it's clear that unmet needs remain. It's gratifying to see that Biogen is continuing to identify the full therapeutic benefit that SPINRAZA can bring to SMA patients through the ASCEND, RESPOND and DEVOTE studies. We look forward to seeing the results of the ASCEND study, which may help inform the future of SMA treatment for patients who are not responding adequately to risdiplam," said C. Frank Bennett Ph.D., Ionis' executive vice president, chief scientific officer and head of the neurology franchise.

KEY TAKEAWAY

"It's gratifying to see that Biogen is continuing to identify the full therapeutic benefit that SPINRAZA can bring to SMA patients through the ASCEND, RESPOND and DEVOTE studies. We look forward to seeing the results of these studies, which are designed to bring additional therapeutic benefit to SMA patients."

- C. Frank Bennett, Ionis' executive vice president, chief scientific officer and head of the neurology franchise

Dr. Bennett noted that the long-term safety and efficacy profile of SPINRAZA across SMA patients of all ages, including some patients treated for up to seven years, supports evaluation of an investigational higher dose of nusinersen in the DEVOTE and ASCEND clinical studies.

Dr. Bennett and Adrian R. Krainer, Ph.D., of Cold Spring Harbor Laboratory, are 2019 co-recipients of the prestigious Breakthrough Prize and the 23rd Jacob and Louise Gabbay Award in Biotechnology and Medicine for their discovery of nusinersen. Dr Bennett is also the recipient of the 2018 Leslie Gehry Brenner Prize for Innovation in Science and the inaugural Healy Center International Prize for Innovation in amyotrophic lateral sclerosis (ALS).

ASCEND is planned to be an approximately 2.5-year study that will enroll up to 135 later-onset, non-ambulatory individuals with SMA (aged 5 to 39). Enrollment is expected to start later in 2021.

SPINRAZA was also highlighted in multiple Biogen-sponsored presentations during the WMS (World Muscle Society) 2021 Virtual Congress, Sept. 20 – 24. The presentations, which further support the efficacy and safety of SPINRAZA, include:

- Scientific Rationale for a Higher Dose of Nusinersen
- Preserved Swallowing Function in Infants Who Initiated Nusinersen Treatment in the Presymptomatic Stage SMA: Results from the NURTURE Study
- Part A Results from the Ongoing DEVOTE Study to Explore Higher-Dose Nusinersen in SMA
- Nusinersen in Children with Spinal Muscular Atrophy (SMA) Who Received Onasemnogene Abeparvovec: Design of the Phase 4 Open-Label RESPOND Study
- Phosphorylated Neurofilament Heavy Chain Level is Associated with Future Motor Function in Nusinersen-treated Individuals with Infantile-Onset SM
- Assessment of Current Best-Practices to Triage and Expedite Incoming Referrals for the Evaluation of Spinal Muscular Atrophy
- Evaluating Perceived Fatigue Within an Adult SMA Population
- CT-Guided Nusinersen Injection Techniques in Patients with SMA

In addition to the presentations at WMS, there are also two posters being presented that are supported by Biogen:

- A Spinal Muscular Atrophy Registry for Real-World Evidence
- TREAT-NMD Core Dataset: An Important Tool for Post-marketing Surveillance