MARCH 28, 2022

Biogen and Ionis Announce Topline Phase 1 Study Results of Investigational Drug in C9orf72 Amyotrophic Lateral Sclerosis

- BIIB078, an investigational antisense oligonucleotide for C9orf72-associated amyotrophic lateral sclerosis (ALS), did not show clinical benefit; clinical program will be discontinued
- Biogen and Ionis remain committed to their decade-long pursuit of advancing ALS research and developing therapies for all forms of this progressive and fatal neurodegenerative disease

Biogen and Ionis Pharmaceuticals today announced topline results from the Phase 1 study of BIIB078 (IONIS-$C9_{Rx}$), an investigational antisense oligonucleotide (ASO) for people with C9orf72-associated amyotrophic lateral sclerosis (ALS).

In this Phase 1 study, BIIB078 was generally well-tolerated. The adverse events (AEs) were mostly mild to moderate in severity and occurred at a similar rate across BIIB078 and placebo groups. The most common AEs were fall, procedural pain and headache.

BIIB078 did not meet any secondary efficacy endpoints and it did not demonstrate clinical benefit. In the dose cohorts up to 60 mg there were no consistent differences between the BIIB078 group and the placebo group. Participants in the BIIB078 90 mg dose cohort trended toward a greater decline than those in the placebo group across secondary endpoints. Based on these results, the BIIB078 clinical development program will be discontinued, including its ongoing open-label extension study.

“We are incredibly grateful for the selfless commitment of the individuals with ALS who participated in the study, and the community’s dedication to advancing research for this devastating disease,” said Toby Ferguson, M.D., Ph.D., Vice President and

Head of the Neuromuscular Development Unit at Biogen. “While these were not the results we were hoping for, they are clear and will inform future research across our broad pipeline of investigational ALS therapies. We remain focused on pioneering new treatments that will positively impact people living with this debilitating disease.”

“C9orf72-associated ALS is a complex genetic form of ALS and there are multiple mechanisms by which the scientific community believes the *C9orf72* gene causes disease. We designed BIIB078 to test the prevailing hypothesis that the mechanisms of disease for C9orf72-associated ALS were caused by toxicity associated with the repeat containing RNA and corresponding dipeptides. Unfortunately, this Phase 1 study did not support the hypothesis, suggesting that the disease mechanism is much more complex. While these results do not support further development of BIIB078, we anticipate they will provide valuable learnings that lead to a deeper understanding of this form of ALS,” said C. Frank Bennett, Executive Vice President, Chief Scientific Officer and Franchise Leader for Neurological Programs at Ionis.

This Phase 1 study was a randomized, placebo-controlled, dose-escalating trial to evaluate BIIB078 administered intrathecally to adults (n=106) with C9orf72-associated ALS. Within each of the six study treatment cohorts, participants were randomized to receive BIIB078 or placebo (3:1 ratio). The primary objective of the study was to assess safety and tolerability. Secondary efficacy endpoints included ALS Functional Rating Scale–Revised, Slow Vital Capacity, Hand-Held Dynamometry, and the Iowa Oral Pressure Instrument.

The companies will present the BIIB078 Phase 1 data at a future scientific forum.

Source: **Globe Newswire**

EUpALS
Kapucijnenvoer 33 B/1, B-3000 Leuven, Belgium
Tel: +32 (0)16-23 95 82 – Fax: +32 (0)16-29 98 65
info@ALS.eu – ALS.eu