Date: January 23, 2025

To: Cure SMA
From: Biogen Patient Advocacy
Subject: Biogen Provides Regulatory Update for Investigational 50/28 mg Dose Regimen of Nusinersen for SMA

Dear Cure SMA & the SMA Community,

In response to your request, we are writing to let you know Biogen announced that the U.S. Food and Drug Administration (FDA) accepted our supplemental New Drug Application (sNDA) for an investigational 50/28 mg dosing regimen of nusinersen for the treatment of SMA in infants, children and adults. The investigational 50/28 mg dosing regimen starts with two 50 mg doses given 14 days apart, followed by 28 mg doses every 4 months.

What study supports the submission to the FDA?
The FDA filing submission included data from the Phase 2/3 DEVOTE study, a three-part study that enrolled 145 patients across all ages and SMA types:

- **Part A:** an open-label safety evaluation period in children and teens (n=6) with later-onset SMA.
- **Part B:** a cohort with infantile onset-symptoms (n=75) and a later-onset cohort (n=24).
- **Part C:** an open-label evaluation in children and adults who transitioned from the approved dose of 12 mg to the 50/28 mg regimen (n=40).

The study, which met its primary endpoint, measured the change from baseline on the Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND) at six months in untreated, symptomatic, infantile-onset patients, compared to a prespecified untreated group from the previous Phase 3 ENDEAR study.

Will there be an expanded access program for the 50/28 mg dosing regimen of nusinersen?
Before the FDA makes its decision on our application, access to investigational higher dose nusinersen is not available outside of the ongoing extension study (ONWARD), which includes participants that completed DEVOTE.

We are committed to supporting individuals with SMA and their families by advancing research that aims to answer critical questions for the community. We are deeply appreciative of the patients, caregivers, and investigators who participated in the DEVOTE study and acknowledge the vital role they play in advancing SMA research.

While the FDA is the regulatory agency that approves the marketing of medicines in the U.S., we are also engaging with regulatory agencies in other countries, as well. Upon your request, we will provide additional updates on the nusinersen program as we are able.

Sincerely,

Your Team at Biogen

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