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MEDIA UPDATE

Novartis announces *Nature Medicine* publication of Zolgensma data demonstrating age-appropriate milestones when treating children with SMA presymptomatically

- *Nearly all children with two and three copies of the SMN2 gene treated presymptomatically achieved age-appropriate milestones, including sitting, standing and walking. All children were free of respiratory and nutritional support, and serious, treatment-related adverse events*
- *Data from 29 patients treated in SPR1NT trial reinforce transformational benefit of early treatment with one-time gene therapy when compared to natural history*
- *More than 2,000 patients have now been treated with Zolgensma globally across clinical trials, managed access programs and in the commercial setting*

Basel, June 17, 2022 - Novartis today announced that *Nature Medicine* published final results from both the two- and three-copy cohorts of the completed Phase 3 SPR1NT trial as separate companion manuscripts, reinforcing the transformational benefit of Zolgensma® (onasemnogene abeparvovec) when used early. These data demonstrate that, whether they have two or three copies of the *SMN2* gene, nearly all children with spinal muscular atrophy (SMA) treated presymptomatically with Zolgensma were able to achieve age-appropriate motor milestones, including sitting independently, standing and walking.[1,2] The final results from the two-and three-copy cohort were presented during the European Academy for Neurology Virtual Congress in 2021, and the 2022 Muscular Dystrophy Association (MDA) Clinical and Scientific Conference, respectively.

The data represent a significant contrast to the natural history of SMA, a devastating disease affecting approximately one in 10,000 infants worldwide. If left untreated, patients with two copies of the *SMN2* gene typically develop SMA Type 1, which leads to progressive and irreversible loss of motor function and, in most cases, death or permanent ventilation by the age of two years.[3,4] Most children with three copies of the *SMN2* gene develop SMA Type 2, characterized by the inability to walk independently.

“The robust data from both the two- and three-copy SPR1NT cohorts are being published together for the first time, further supporting the significant and clinically meaningful benefit of Zolgensma in presymptomatic babies with SMA,” said Shephard Mpofu, M.D., SVP, Chief Medical Officer, Novartis Gene Therapies. “When treated with Zolgensma prior to the onset of symptoms, not only did all 29 patients enrolled in SPR1NT survive, but were thriving — breathing and eating on their own, with most even sitting, standing and walking without assistance.”

The results from the SPR1NT study showed that, remarkably:

- All children (100 percent) treated presymptomatically in the SPR1NT two-copy cohort met the primary endpoint of sitting independently for ≥30 seconds, including 11/14 (79

percent) who achieved this milestone within the World Health Organization (WHO) window of normal development. A majority of patients went on to stand independently (11/14) and walk independently (9/14), most within the typical range of normal development.[1]

- In the three-copy cohort of SPR1NT, 14/15 children (93 percent) went on to walk independently, most (11/15, 73 percent) within the WHO window of normal development. All 15 children (100 percent) met the primary endpoint of standing alone ≥3 seconds, including 14/15 (93 percent) within the WHO window of normal development.[2]
- Reported adverse reactions were consistent with previous data, with no new safety signals identified.
- Patients enrolled in SPR1NT are invited for long-term follow-up study to collect additional safety and efficacy data; associated updates evaluating motor function gains will be published later this year.

Parents Amy and Adan Medina enrolled their daughter Amelia in the SPR1NT trial upon birth, after an amniocentesis during pregnancy confirmed Amelia had SMA Type 1. The family sought to test for the disease early after the Medina's first two children were diagnosed with SMA years prior. Amelia was the first child treated as part of the trial, at 11 days old.

"Amelia has met all of her motor milestones on time, and is sitting, standing and walking independently. She is indistinguishable from her healthy peers without SMA," Amy said. "This is especially meaningful to our family as our older two children with SMA were born before treatment with a one-time gene therapy was even a possibility."

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About Zolgensma
Zolgensma® (onasemnogene abeparvovec) is the only approved gene therapy for the treatment of spinal muscular atrophy (SMA) and the only SMA treatment designed to directly address the genetic root cause of the disease by replacing the function of the missing or non-working *SMN1* gene to halt disease progression through sustained SMN protein expression with a single, one-time IV infusion. Zolgensma is now approved in more than 40 countries and more than 2,000 patients have been treated with Zolgensma globally across clinical trials, managed access programs, and in the commercial setting.[5] Novartis Gene Therapies is unwavering in its commitment to reimagine the possibilities for children living with SMA and continues to evaluate Zolgensma across a robust clinical development program, as well as the investigational intrathecal administration of OAV101 in patients with later-onset forms of SMA.

Novartis Gene Therapies has an exclusive, worldwide license with Nationwide Children's Hospital to both the intravenous and intrathecal delivery of AAV9 gene therapy for the treatment of all types of SMA; has an exclusive, worldwide license from REGENXBIO for any recombinant AAV vector in its intellectual property portfolio for the *in vivo* gene therapy treatment of SMA in humans; an exclusive, worldwide licensing agreement with Généthon for *in vivo* delivery of AAV9 vector into the central nervous system for the treatment of SMA; and a non-exclusive, worldwide license agreement with AskBio for the use of its self-complementary DNA technology for the treatment of SMA.

About Spinal Muscular Atrophy
Spinal muscular atrophy (SMA) is a rare, genetic neuromuscular disease and a leading genetic cause of infant death.[6,7] Caused by the lack of a functional *SMN1* gene, the most severe forms of SMA results in the rapid and irreversible loss of motor neurons, affecting muscle functions including breathing, swallowing and basic movement.[4] Severity varies across a spectrum of types corresponding to the number of copies of the back-up *SMN2* gene.[8] The majority (>70 percent) of patients with two copies of *SMN2* develop Type 1, the most common form accounting for 60 percent of cases.[9,10] Type 1 is severe and,

left untreated, leads to death or the need for permanent ventilation by the age of two in more than 90 percent of cases. [6,7] Most patients (>80 percent) with three copies of *SMN2* develop Type 2, accounting for 30 percent of cases.[9] Left untreated, patients with Type 2 are unable to walk and will require a wheelchair, and more than 30 percent will die by age 25.[11] Loss of motor neurons cannot be reversed, so it is imperative to diagnose SMA and begin treatment, including proactive supportive care, as early as possible to halt irreversible motor neuron loss and disease progression.[12,13]

About Novartis Gene Therapies
Novartis Gene Therapies is reimagining medicine to transform the lives of people living with rare genetic diseases. Utilizing cutting-edge technology, we are working to turn promising gene therapies into proven treatments. We are powered by an extensive manufacturing footprint, in capacity and expertise, enabling us to bring gene therapy to patients around the world at quality and scale. Novartis Gene Therapies OAV101 clinical development program represents a growing body of research in a range of patients with SMA, across ages, SMA types and incident and prevalent populations, investigating both intravenous and intrathecal formulations.

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About Novartis
Novartis is reimagining medicine to improve and extend people’s lives. As a leading global medicines company, we use innovative science and digital technologies to create transformative treatments in areas of great medical need. In our quest to find new medicines, we consistently rank among the world’s top companies investing in research and development. Novartis products reach nearly 800 million people globally and we are finding

innovative ways to expand access to our latest treatments. About 108,000 people of more than 140 nationalities work at Novartis around the world. Find out more at https://www.novartis.com.

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