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MEDIA & INVESTOR RELEASE

Novartis data again demonstrate age-appropriate development when Zolgensma is used presymptomatically, and post-hoc data reveal SMA Type 1 patients could speak, swallow and maintain airway protection

- *Children with three copies of SMN2 treated presymptomatically achieved age-appropriate milestones, including standing and walking; required no ventilatory or feeding tube support; and had no serious, treatment-related adverse events*
- *Post-hoc analyses of START, STR1VE-EU and STR1VE-US indicated children with SMA Type 1 achieved or maintained important measures of bulbar function*
- *More than 1,800 patients have now been treated with Zolgensma globally across clinical trials, managed access programs and in the commercial setting*[1]

Basel, March 14, 2022 — Novartis today announced new data that reinforce the transformational benefit of Zolgensma® (onasemnogene abeparvovec), an essential one-time treatment for spinal muscular atrophy (SMA). The completed Phase 3 SPR1NT study demonstrated that children with three copies of the *SMN2* back-up gene who were treated presymptomatically achieved age-appropriate motor milestones, including standing and walking.[2] In addition, a descriptive post-hoc analyses of START, STR1VE-EU and STR1VE-US (n=65) indicated children with SMA Type 1 achieved or maintained important measures of bulbar function following treatment with Zolgensma, including ability to speak; swallow and meet nutritional needs; and maintain airway protection.[3] These data are among a Zolgensma data set being presented during the 2022 Muscular Dystrophy Association (MDA) Clinical and Scientific Conference, which also include, in part, real-world data from the RESTORE registry and a chart review of US patients who changed therapy to Zolgensma.

Without treatment, most children with three copies of the *SMN2* back-up gene develop SMA Type 2, characterized by the inability to walk independently.[2] In contrast, 14/15 children (93 percent) in the three-copy cohort of SPR1NT went on to walk independently, most (11/15, 73 percent) within the World Health Organization (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. All children were free of feeding tube support and ventilatory support of any kind during the study, and no serious, treatment-related adverse events were reported.

“Results from SPR1NT again confirm the remarkable impact of Zolgensma for children at risk for SMA who are treated before the onset of symptoms. In sharp contrast to the natural course of SMA, children treated preemptively with Zolgensma are standing and walking, with few or no signs of neuromuscular disease. Many of these children achieve patterns of motor development indistinguishable from their healthy peers without SMA,” said Kevin Strauss, M.D., Medical Director, Clinic for Special Children in Pennsylvania. “These data clearly

demonstrate the value of newborn screening for SMA, which is vital to affording children the earliest diagnosis and treatment to ensure the best possible outcomes."

Bulbar motor neurons control muscles required for functions like swallowing, speaking and chewing, and impairment from SMA can lead to choking, malnutrition, infection and death.[3] Given there is no widely accepted definition of bulbar function, a post-hoc analyses of children with SMA Type 1 who received Zolgensma in the START, STR1VE-EU and STR1VE-US studies (n=65) defined bulbar function using a composite endpoint including three key components: communication, swallowing and maintenance of airway protection. Of the patients that could be retrospectively and descriptively assessed against all components, 80 percent (16/20) achieved the composite endpoint.

"The effect of SMA Type 1 on bulbar function often leads to debilitating complications, such as increased risk of aspiration, as well as social consequences from impairment of speech development. These post-hoc data suggest Zolgensma can have an important impact on a child's well-being," said Shephard Mpofu, M.D., SVP, Chief Medical Officer, Novartis Gene Therapies. "Additional data presented at MDA continue to reinforce the consistent, significant and clinically meaningful therapeutic benefit of Zolgensma in the real-world setting, including in patients outside of our current clinical trial experience."

Final SPR1NT Three-Copy Cohort Results
SPR1NT is a Phase 3, open-label, single-arm, multi-centre trial designed to evaluate the safety and efficacy of a one-time intravenous infusion of Zolgensma in presymptomatic patients with a genetic diagnosis of SMA and two or three copies of *SMN2* who were ≤6 weeks of age.[2] Mean age at dosing in the three-copy cohort was 28.7 days (9–43 days). Fourteen patients with two copies of *SMN2* and 15 patients with three copies of *SMN2* were treated. Most patients (>80 percent) with three copies of *SMN2* develop SMA Type 2, which accounts for 30 percent of SMA cases.[2] According to natural history, patients with SMA Type 2 never walk independently without intervention.

Three-copy cohort (n=15) final results:

- One hundred percent of patients (15/15) met the primary endpoint of standing unassisted for ≥3 seconds by 24 months of age, including 14 who achieved this milestone within the WHO window of normal development.
- Fourteen patients (93 percent) walked independently, 11 of whom achieved this milestone within the WHO window of normal development.
- All patients (100 percent) were independent of nutritional and respiratory support for the duration of the study.

All patients experienced at least one adverse event (AE) after dosing, eight (53 percent) of which were considered to be treatment-related. There were no serious, treatment-related AEs. Three patients were reported to have had serious adverse events (SAEs), all of which resolved and were not related to treatment.

The final results from the SPR1NT two-copy cohort were presented during the European Academy for Neurology (EAN) Virtual Congress 2021. Additional details on those results can be found here.

Bulbar Function Post-Hoc Analysis
The post-hoc analyses descriptively assessed pooled data from one Phase 1 (START) and two Phase 3 (STR1VE-EU and STR1VE-US) studies to evaluate components of bulbar function in children with symptomatic SMA Type 1 after receiving Zolgensma.[3] Bulbar function was defined as integrity within cranial nerves that enables an individual to speak with comprehension by an unknown listener, swallow food and liquids, and meet nutritional needs while maintaining airway protection. The study retrospectively assessed the percentage of patients who achieved each endpoint and all three endpoints at predetermined times or at the

end of the study (24 months of age in START and 18 months of age in STR1VE-EU and STR1VE-US).

- Overall, 65 patients aged <6 months at time of Zolgensma treatment were analyzed.
- Sixty-five patients were analyzed for swallowing (START [n=11]; STR1VE-EU [n=32]; STR1VE-US [n=22]). Communication was only assessed for patients from native English-speaking families in START and STR1VE-US; not all patients had outcomes for all three measures (START [n=4]; STR1VE-US [n=16]).
- Ninety-five percent (19/20) met the communication endpoint.
- Ninety-two percent (60/65) had at least one occurrence of a normal swallow test.
- Ninety-two percent (60/65) did not report any event indicating the inability to maintain airway protection.
- Overall, 80 percent (16/20) achieved the composite endpoint of having the ability to speak, being able to swallow normally, and maintaining airway protection.

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 1,800 patients have been treated with Zolgensma globally across clinical trials, managed access programs, and in the commercial setting.[1] 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.[4,5] 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.[6] Severity varies across a spectrum of types corresponding to the number of copies of the back-up *SMN2* gene.[7] The majority (>70 percent) of patients with two copies of *SMN2* develop Type 1, the most common form accounting for 60 percent of cases.[8,9] 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.[4,5] Most patients (>80 percent) with three copies of *SMN2* develop Type 2, accounting for 30 percent of cases.[8] 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.[10] 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.[11,12]

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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