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MEDIA & INVESTOR RELEASE

Zolgensma® data including patients with more severe SMA at baseline further demonstrate therapeutic benefit, including prolonged event-free survival, increased motor function and milestone achievement

- *Nearly two-thirds of patients (65.6%) in STR1VE-EU have already achieved developmental motor milestones not observed in the natural history of SMA Type 1 at a mean duration of follow-up of 10.6 months, including patients with a more severe phenotype compared to previous studies*

- *Two-thirds of patients (66.7%) were free of feeding support, an important indicator of stabilization/halting of disease progression*

- *New interim Phase 3 STR1VE-EU data presented at WMS support the robust clinical evidence that have demonstrated a consistent, transformative benefit across Zolgensma clinical trials for the treatment of patients with SMA*

- *More than 600 patients now treated with Zolgensma, including some more than five years post-treatment and more than five years old*

Basel, October 1, 2020 – Novartis Gene Therapies today announced new interim data from the ongoing Phase 3 STR1VE-EU clinical trial for Zolgensma® (onasemnogene abeparvovec) that demonstrated patients with spinal muscular atrophy (SMA) Type 1 continued to experience significant therapeutic benefit, including event-free survival, rapid and sustained improvement in motor function and motor milestone achievement, including for some patients with more aggressive disease at baseline compared to previous trials. SMA is a rare, genetic neuromuscular disease caused by a lack of a functional *SMN1* gene that results in the progressive and irreversible loss of motor neurons, affecting muscle functions, including breathing, swallowing, and basic movement.[1,2,3] These data as of December 31, 2019, and presented today during a virtual Clinical Trial Poster Session as part of the World Muscle Society (WMS) 2020 Virtual Congress, support the robust clinical evidence that has demonstrated a consistent, transformative benefit across Zolgensma clinical trials for the treatment of patients with SMA.

“We are seeing further evidence of the potential of Zolgensma to effectively halt motor neuron loss following a one-time, intravenous infusion. In STR1VE-EU, patients achieved rapid improvements in motor function following treatment with Zolgensma, and most have already achieved motor milestones not observed in the natural history of SMA Type 1,” said Professor Eugenio Mercuri, M.D., PhD., Department of Pediatric Neurology, Catholic University, Rome, Italy. “These interim results are especially encouraging considering STR1VE-EU includes some patients with a more severe phenotype than in the START and STR1VE-US studies,

further supporting the gene therapy's positive benefit/risk profile, even in this more fragile population."

"These strong interim results from the STR1VE-EU clinical trial continue to demonstrate consistent and significant therapeutic benefit in patients with SMA Type 1, the most common form of the disease, adding to the robust body of clinical evidence for Zolgensma," said Shephard Mpofu, M.D., SVP, Chief Medical Officer, Novartis Gene Therapies. "With more than 600 patients now treated, including some more than five years post-treatment and more than five years old, these data further reinforce the transformative benefit a one-time dose of Zolgensma has on SMA patients."

Phase 3 STR1VE-EU Data as of December 31, 2019
STR1VE-EU is designed to evaluate the efficacy and safety of a single, one-time IV infusion of Zolgensma in patients with SMA Type 1 who are less than six months of age at the time of gene therapy, with one or two copies of the *SMN2* backup gene and who have bi-allelic *SMN1* gene deletion or point mutations. The mean age of dosing was 4.1 months and the mean age at the onset of symptoms was 1.6 months. The mean Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND) score at baseline was 28. Thirty-one of 33 patients (93.9%) were able to swallow thin liquids, and 10 patients (30.3%) required feeding support at baseline. Nine of thirty patients (27.3%) required ventilatory support at baseline. STR1VE-EU is distinct in its inclusion and exclusion criteria and baseline clinical characteristics of enrolled patients compared with START or STR1VE-US. Specifically, some patients in STR1VE-EU had a more severe disease phenotype at baseline, including lower CHOP-INTEND scores and the need for nutritional and ventilatory support.

At last visit before the data cutoff, patients in STR1VE-EU were between 6.9 and 18.6 months of age, and mean duration in the study was 10.6 (1.8–15.4) months. Thirty-one out of 32 (97%) patients in the intent-to-treat (ITT) population survived event-free, including 30 (93.8%) who could have reached 10.5 months of age and 18 (56.3%) who could have reached 13.6 months of age. An event is defined as the need for tracheostomy or the requirement of ≥16 hours of respiratory assistance per day (via non-invasive ventilatory support) for ≥14 consecutive days in the absence of an acute reversible illness, excluding peri-operative ventilation. Untreated natural history indicates that only 50% and 25% of babies with SMA Type 1 will survive event-free by the time they reach 10.5 months of age and 13.6 months of age, respectively.[3]

Twenty-one patients (65.6%) achieved motor milestones not observed in the natural history of SMA Type 1. This includes six patients (18.8%) who could sit independently for ≥10 seconds (the primary efficacy endpoint), 20 patients (66.7%) who gained head control, eight patients (25%) who were able to roll from back to sides and one patient who could stand with assistance, crawl and walk with assistance. The mean increase in CHOP INTEND from baseline was 5.9 points (n=31) which was observed as early as at one month post-dosing, 10.1 points at 3 months (n=29) post-dosing, and 13.3 points at six months (n=27) post-dosing. Twenty-one children (65.6%) enrolled in STR1VE-EU achieved and maintained a CHOP INTEND score of ≥40 points and 12 children (37.5%) were able to achieve a score of ≥50. According to natural history, untreated patients with SMA Type 1 almost never achieve a CHOP INTEND score ≥40.[3,4]

The majority (91.7%) of patients who were free of ventilatory support at baseline remained either completely free of ventilatory support or received prophylactic BiPAP support during the study for acute reasons. Two-thirds (66.7%) of patients in the ITT population were able to feed orally without the need for feeding support, an important indicator of stabilization/halting of disease progression.

As previously reported, one patient discontinued the study because of a serious adverse event of hypoxic-ischemic brain damage and respiratory distress that resulted in death.

Novartis and the investigator considered the events and death to be unrelated to treatment with Zolgensma based on autopsy findings. Thirty-two of 33 patients were reported to have at least one adverse event (AE), of which six patients experienced serious adverse events that were considered by the investigator to be related to Zolgensma. Liver transaminase elevations, some of which were reported as adverse events, were experienced by 29 of 33 patients (87.9%), but all resolved with the use of prednisolone. Four patients had reported decreases in platelet counts <75,000, three of which were isolated laboratory abnormalities without adverse events reported. Overall, no new safety signals have been identified and the reported adverse events are consistent with the cumulative safety profile with Zolgensma.

Novartis Gene Therapies is grateful to the courageous patients and families who participate in clinical trials, enabling the company to further its efforts to make a meaningful difference in the lives of patients with rare genetic diseases.

About Zolgensma® (onasemnogene abeparvovec)
Zolgensma® is designed to address the genetic root cause of SMA by providing a functional copy of the human SMN gene to halt disease progression through sustained SMN protein expression with a single, one-time IV infusion. Zolgensma was approved by the U.S. Food and Drug Administration in May 2019 and represents the first approved therapeutic in Novartis Gene Therapies' proprietary platform to treat rare, monogenic diseases using gene therapy.[5] In addition to the United States, Zolgensma is approved in Japan, Europe and Brazil. More than 600 patients have been treated with Zolgensma, including clinical trials, commercially and through the managed access program. Novartis Gene Therapies is pursuing registration in close to three dozen countries with regulatory decisions anticipated in Switzerland, Canada, Israel, Australia, and South Korea in late-2020 or early 2021.[5]

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
SMA is the leading genetic cause of infant death.[1,2] If left untreated, SMA Type 1 leads to death or the need for permanent ventilation by the age of two in more than 90% of cases.[3,4] SMA is a rare, genetic neuromuscular disease caused by a lack of a functional *SMN1* gene, resulting in the rapid and irreversible loss of motor neurons, affecting muscle functions, including breathing, swallowing and basic movement.[1] 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.[5] This is especially critical in SMA Type 1, where motor neuron degeneration starts before birth and escalates quickly. Loss of motor neurons cannot be reversed, so SMA patients with symptoms at the time of treatment will likely require some supportive respiratory, nutritional and/or musculoskeletal care to maximize functional abilities.[6] More than 30% of patients with SMA Type 2 will die by age 25.[7]

About Novartis Gene Therapies
Novartis Gene Therapies (formerly AveXis) is reimagining medicine to transform the lives of people living with rare genetic diseases. Utilizing cutting-edge technology, we are turning promising gene therapies into proven treatments, beginning with our transformative gene therapy for spinal muscular atrophy (SMA). This therapy is now approved in the U.S., Japan, Europe and Brazil, and additional registrations are being pursued in close to three dozen countries, with regulatory decisions anticipated in Switzerland, Canada, Israel, Australia, Argentina and South Korea in late 2020 or early 2021. Our robust AAV-based pipeline is advancing treatments for Rett syndrome; a genetic form of amyotrophic lateral sclerosis (ALS) caused by mutations in the superoxide dismutase 1 *(SOD1)* gene; and Friedreich's ataxia. We

are powered by the world's largest gene therapy manufacturing footprint of more than one million square feet, enabling us to bring these therapies to patients around the world at quality and scale.

Disclaimer

This press release contains forward-looking statements within the meaning of the United States Private Securities Litigation Reform Act of 1995. Forward-looking statements can generally be identified by words such as "potential," "can," "will," "plan," "may," "could," "would," "expect," "anticipate," "seek," "look forward," "believe," "committed," "investigational," "pipeline," "launch," or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for the investigational or approved products described in this press release, or regarding potential future revenues from such products. You should not place undue reliance on these statements. Such forward-looking statements are based on our current beliefs and expectations regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. There can be no guarantee that the investigational or approved products described in this press release will be submitted or approved for sale or for any additional indications or labeling in any market, or at any particular time. Nor can there be any guarantee that such products will be commercially successful in the future. In particular, our expectations regarding such products could be affected by, among other things, the uncertainties inherent in research and development, including clinical trial results and additional analysis of existing clinical data; regulatory actions or delays or government regulation generally; global trends toward health care cost containment, including government, payor and general public pricing and reimbursement pressures and requirements for increased pricing transparency; our ability to obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; general political, economic and business conditions, including the effects of and efforts to mitigate pandemic diseases such as COVID-19; safety, quality, data integrity or manufacturing issues; potential or actual data security and data privacy breaches, or disruptions of our information technology systems, and other risks and factors referred to in Novartis AG's current Form 20-F on file with the US Securities and Exchange Commission. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

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 109,000 people of more than 140 nationalities work at Novartis around the world. Find out more at https://www.novartis.com.

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