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## MEDIA UPDATE

# Novartis to initiate SMART Phase 3b global study of Zolgensma in children up to 21 kg, building on real-world experience

- *SMART study to extend data beyond patient population studied in clinical trials*

- *New clinical study to evaluate safety and efficacy of Zolgensma in children up to 21 kg, adding to real-world experience and regulatory approvals in Europe and Canada*

**Basel, April 23, 2021** — Novartis today announced plans to initiate SMART, a Phase 3b clinical study to evaluate the safety and efficacy of Zolgensma® (onasemnogene abeparvovec) in young children with spinal muscular atrophy (SMA) weighing ≥ 8.5 kg and ≤ 21 kg, following a one-time, intravenous (IV) infusion. The new clinical data will supplement emerging real-world evidence and use of this innovative therapy in the European Union and Canada, where regulatory approval includes dosing guidance for babies and young children up to 21 kg. Since launch, more than half (55 percent) of children treated in Europe range in weight between ≥ 8.5 kg and ≤ 21 kg. According to Pediatric Neuromuscular Clinical Research's (PNCR) natural history study of SMA, almost all patients under the age of five years will be under 21 kg, with some patients as old as eight years of age weighing below 21 kg.

The global study is expected to enroll 24 symptomatic children with SMA across sites in Europe, North America, Australia and Taiwan, and will follow patients for a period of 12 months. Enrollment is anticipated to start in September 2021, with targeted recruitment led by the individual sites. Additional details on the SMART study can be found on clinicaltrials.gov.

"With more than 1,000 patients treated globally to date, we have seen the transformative impact of Zolgensma and are committed to making our essential, one-time gene therapy available to all patients with SMA who may benefit," said Shephard Mpofu, M.D., SVP, Chief Medical Officer, Novartis Gene Therapies. "SMART will expand the clinical evidence beyond the patient population studied in Zolgensma trials to date, and provide the SMA community valuable data on its use in children up to 21 kg. These data will add to the strong interest and emerging real-world use and evidence we have seen to date, with a goal of enabling confidence among caregivers, healthcare professionals and regulatory authorities as they make informed treatment decisions."

Zolgensma has demonstrated significant and clinically meaningful therapeutic benefit in pre-symptomatic and symptomatic SMA, including prolonged event-free survival and achievement of motor milestones unseen in natural history of the disease and, to date, sustained for more than five years post-dosing in children now up to six years of age. The Zolgensma clinical

program has studied symptomatic children less than six months of age with SMA Type 1 in the clinical setting, but emerging findings from the RESTORE registry, recently presented at the 2021 Muscular Dystrophy Association (MDA) Virtual Clinical and Scientific Conference, indicate older children (≥ 6 months) achieved a clinically meaningful benefit when treated with Zolgensma alone, after switching to gene therapy or in combination with another SMA therapy, with safety events consistent with the previously described safety profile. RESTORE is designed to provide real-world data for enhancing our understanding of patients cared for in routine clinical practice.

“SMART is a study designed to expand the clinical evidence for Zolgensma in children up to 21 kg,” said Nicole Gusset, PhD, President of SMA Europe. “We have seen the interest in Zolgensma among physicians and families across Europe, and believe this additional safety and efficacy data will help the community better understand its potential and inform treatment decisions for young children with SMA.”

**About SMART**
SMART is a Phase 3b, open-label, single-arm, multicenter study designed to evaluate the safety, tolerability and efficacy of a one-time IV infusion of Zolgensma in pediatric patients who have symptomatic SMA with bi-allelic mutations in the *SMN1* gene and any copy number of the *SMN2* gene and weigh ≥ 8.5 kg and ≤ 21 kg. The study is expected to enroll 24 patients and will follow participants for a period of 12 months. After study completion, eligible participants will be invited to enroll into a long-term, follow-up study to collect additional safety and efficacy data.

The study’s primary endpoint of key safety assessments will include evaluation of adverse events, laboratory data, vital signs and cardiac safety monitoring. Secondary efficacy endpoints will be assessed as a change from baseline in achievement of motor milestones according to the World Health Organization-Multicentre Growth Reference Study (WHO-MGRS), Bayley Scales of Infant and Toddler Development-Third Edition (Bayley-III) criteria, Hammersmith Functional Motor Scale - Expanded (HFMSE) and the Revised Upper Limb Module (RULM), as appropriate according to participant age.

**About Zolgensma® (onasemnogene abeparvovec)**
Zolgensma® (onasemnogene abeparvovec) is the only gene therapy for 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 SMN gene to halt disease progression through sustained SMN protein expression with a single, one-time IV infusion. Zolgensma represents the first approved therapeutic in Novartis Gene Therapies’ proprietary platform to treat rare, monogenic diseases using gene therapy. Zolgensma was approved in the U.S. in May 2019 and subsequently has been approved in 39 countries. To date, more than 1,000 patients have been treated with Zolgensma across clinical trials, managed access programs, and in the commercial setting.[1]

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)**
SMA is the leading genetic cause of infant death.[2,3] 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.[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.[2] 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.[5,6] 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.[6,7] More than 30% of patients with SMA Type 2 will die by age 25.[8]

**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 working to turn promising gene therapies into proven treatments, beginning with our transformative gene therapy for spinal muscular atrophy (SMA). Our robust AAV-based pipeline is advancing treatments for Rett syndrome and Friedreich's ataxia. We are powered by the world's largest, commercially-proven gene therapy manufacturing footprint, enabling us to bring gene therapy to patients around the world at quality and scale.

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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 110,000 people of more than 140 nationalities work at Novartis around the world. Find out more at https://www.novartis.com.

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**References**


1. Data on file.
2. Sugarman EA, Nagan N, Zhu H, et al. Eur J Hum Genet. 2012;20(1):27-32.
3. Kolb SJ, Coffey CS, Yankey JW, et al. Ann Neurol. 2017;82(6):883-891.
4. Finkel RS., et al. Neurology. 2014;83(9):810-817.
5. Soler-Botija C, et al. Brain. 2002;125(7):1624-1634.
6. Glascock J, Sampson J, Haidet-Phillips A, et al. J Neuromuscul Dis. 2018;5:145-158.
7. Wang CH, et al. J Child Neurol. 2007;22(8):1027-1049.
8. Darras BT, Finkel RS. Spinal Muscular Atrophy. Chapter 25 - Natural History of Spinal Muscular Atrophy. October 2017.


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