EMBARGOED UNTIL 00:01 Monday 8th March 2021

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Landmark agreement enables families in England to have access to innovative one-time gene therapy on the NHS

- *NHS England and Novartis Gene Therapies have concluded a landmark agreement that secures access for families in England to Zolgensma®▼ (onasemnogene abeparvovec), the only one-time gene therapy for spinal muscular atrophy (SMA).*
- *The announcement of this agreement coincides with NICE draft guidance recommending onasemnogene abeparvovec as a treatment option on the NHS.*
- *Onasemnogene abeparvovec is the only therapy designed to address the genetic root cause of SMA helping to halt disease progression.*[1]

London, UK, 8th March, 2021 NHS England (NHSE) and Novartis Gene Therapies have concluded a landmark agreement that enables access to Zolgensma® (onasemnogene abeparvovec) for use in the NHS in England for infants with a clinical diagnosis, or a genotype predictive, of spinal muscular atrophy (SMA) Type 1. The terms of the agreement build on draft recommendations issued today by the National Institute for Health and Clinical Excellence (NICE) to expedite access for patients whilst NICE final guidance is concluded. Additionally, children with Type 1 SMA who currently fall outside these draft recommendations, but are within the scope of the marketing authorisation, can be considered for treatment by the national multidisciplinary team; where it determines that treatment with onasemnogene abeparvovec would be clinically appropriate, then NHS England will reimburse the costs.

Untreated SMA is the leading genetic cause of infant death[2,3] and is a rare, inherited, 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] Untreated SMA Type 1 leads to death or the need for permanent ventilation by the age of two in more than 90% of cases.[4,5]

Professor Francesco Muntoni, Director of the Dubowitz Neuromuscular Centre at the UCL Great Ormond Street Institute of Child Health and Great Ormond Street Hospital Trust, London commented, *"This important new advice will enable clinicians in England to have access to this extremely promising novel therapy, which will have a major positive impact for the lives of babies and children diagnosed with this devastating neurodegenerative condition, by addressing its genetic root. Having seen first-*

hand the impact of severe SMA on infants and their families, this decision offers a glimpse of the potential of one-time gene therapy to replace the burden of years of repeated chronic treatments or palliative care."

Onasemnogene abeparvovec is the first one-time gene therapy for any neuromuscular condition and works by replacing the function of the faulty *SMN1* gene. In clinical trials, it has demonstrated significant and clinically meaningful therapeutic benefit in pre-symptomatic and symptomatic SMA Type 1, including prolonged event-free survival and achievement of motor milestones, unseen in the natural history of the disease and sustained for more than five years post-dosing and with a manageable safety profile.[6-9]

"This ground-breaking gene therapy offers real hope for the future. We truly welcome this decision, so parents in England whose children are covered by this agreement will now be able to discuss a choice of NHS-funded drug treatments with their clinician," added Liz Ryburn, Support Services Manager of community support and advocacy organisation Spinal Muscular Atrophy UK. *"We will continue to advocate for this therapy to be fully accessible as a treatment option in the UK for all children for whom it is clinically safe and potentially beneficial."*

Novartis Gene Therapies has worked closely with both NHSE and NICE during the NICE Highly Specialised Technologies (HST) appraisal of the cost-effectiveness of Zolgensma and will continue to do so until its conclusion, and beyond, to seek to ensure that all families in England that can benefit from onasemnogene abeparvovec will have access.

Sally-Anne Tsangarides, General Manager at Novartis Gene Therapies in the UK, commenting on the decision said, *"We thank the entire SMA community of families and clinicians for their efforts to help NICE and NHS England appreciate the unmet need in SMA. We are delighted for them that Zolgensma will soon become available to the families in England who need it. Breathing and feeding independently, and developmental milestone achievements like sitting and standing, which have been seen in infants treated with a one-time dose of Zolgensma in clinical studies, are unprecedented in the natural history of the disease."*

Onasemnogene abeparvovec has conditional marketing authorisation and is indicated for the treatment of patients with 5q SMA with a bi-allelic mutation in the *SMN1* gene and a clinical diagnosis of SMA Type 1, or patients with 5q SMA with a bi-allelic mutation in the *SMN1* gene and up to 3 copies of the *SMN2* gene.[1]

Product information is available at: Summary of Product Information for Zolgensma

Notes to Editors

The Scottish Medicines Consortium (SMC) is due to publish its assessment on 8th March 2021.

About 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.[4,5] 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.[9] 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 maximise functional abilities.[10]

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 was approved in May 2019 by the US Food and Drug Administration and represents the first approved therapeutic in Novartis Gene Therapies' innovative proprietary platform born to treat rare monogenic diseases using gene therapy.[11] In addition to the United States, Zolgensma has been approved in over 38 countries. To date, more than 1,000 patients have been treated with Zolgensma worldwide across clinical trials, managed access programmes, and in the commercial setting.

Novartis Gene Therapies has an exclusive, worldwide licence 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 licence 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 licence agreement with AskBio for the use of its self-complementary DNA technology for the treatment of SMA.

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 gene therapy manufacturing footprint of more than one million square feet, enabling us to bring gene therapy to patients around the world at quality and scale.

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March 2021
UK-UNB-21-0035

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