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Novartis receives approval from Japanese Ministry of Health, Labour and Welfare for Zolgensma® the only gene therapy for patients with spinal muscular atrophy (SMA)

- *Zolgensma® (onasemnogene abeparvovec), a one-time administered gene therapy, is approved for the treatment of SMA in patients under the age of two, including those who are pre-symptomatic at diagnosis*

- *Zolgensma has demonstrated significant and clinically meaningful therapeutic benefit in symptomatic and pre-symptomatic SMA, including prolonged event-free survival and achievement of motor milestones unseen in natural history of the disease*

- *Designated as an intractable disease in Japan, SMA is the leading genetic cause of infant death and, if left untreated in its most common form (Type 1), leads to death or the need for permanent ventilation by the age of two in more than 90% of cases*[1,2]

- *Reimbursement with MHLW is expected by the end of 1H20, pending agreement, Zolgensma will be available at that time*

Basel, March 19, 2020 — Novartis Pharma K.K. ("Novartis Pharma") today announced that the Japanese Ministry of Health, Labour and Welfare (MHLW) approved Zolgensma® (onasemnogene abeparvovec) for the treatment of spinal muscular atrophy (SMA) in patients under the age of two, including those who are pre-symptomatic at diagnosis. Patients must be negative for elevated anti-AAV9 antibodies. A rare, genetic neuromuscular disease caused by a lack of a functional *SMN1* gene, SMA results in the rapid and irreversible loss of motor neurons, affecting muscle functions, including breathing, swallowing and basic movement.[3] Approximately 60% of all SMA is Type 1. Zolgensma is a one-time gene therapy designed to address the genetic root cause of the disease by replacing the function of the missing or nonworking *SMN1* gene. Zolgensma is administered during a single intravenous (IV) infusion, delivering a new working copy of the SMN gene into a patient's cells, halting disease progression. Approximately 15-20 SMA patients in Japan are expected to be eligible for treatment each year. Reimbursement with MHLW is expected by the end of 1H20 and, pending agreement, Zolgensma will be available at that time.

"SMA is the leading genetic cause of infant death and, if left untreated in its most common form, Type 1, leads to death or the need for permanent ventilation by the age of two in more than 90% of cases," said Kazunari Tsunaba, president and representative director, Novartis Pharma. "A one-time dose of Zolgensma has the potential to make a truly transformative impact on this life-threatening disease. This is an important day for the children and families in Japan impacted by SMA, both today and in the future."

Approval is based on the Phase 1 START, START Long-term follow-up, Phase 3 STR1VE-US, Phase 3 SPR1NT and Phase 1/2 STRONG (intrathecal injection) trials. START and STR1VE-US were designed to evaluate the efficacy and safety of a one-time IV infusion of Zolgensma in symptomatic SMA Type 1 patients <6 months of age at dosing, who had one or two copies of the *SMN2* backup gene, or two copies of the *SMN2* backup gene, respectively. Zolgensma demonstrated rates of survival never seen in the natural history of the disease; rapid motor function improvement, often within one month of dosing; and milestone achievement, including the ability to sit without support, a milestone never achieved in untreated patients. Patients in START Long-term follow-up are now reaching five years of age. Interim results from the ongoing SPR1NT trial, a Phase 3, open-label, single-arm study of a single, one-time IV infusion of Zolgensma in pre-symptomatic patients (<6 weeks at age of dosing) genetically defined by bi-allelic deletion of *SMN1* with 2 or 3 copies of *SMN2* demonstrate rapid, age-appropriate major milestone gain, reinforcing the critical importance of early intervention in SMA patients. 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.

The most commonly observed side effects after treatment were elevated liver enzymes and vomiting. Acute serious liver injury and elevated aminotransferases can occur. Patients with pre-existing liver impairment may be at higher risk. Prior to infusion, physicians should assess liver function of all patients by clinical examination and laboratory testing. And, they should administer systemic corticosteroid to all patients before and after treatment, and then continue to monitor liver function for at least 3 months after infusion.

“Zolgensma provided rapid, significant and clinically meaningful therapeutic benefit in symptomatic and pre-symptomatic SMA, including prolonged event-free survival and achievement of motor milestones never seen before in natural history of the disease. We are proud to bring the first gene therapy for SMA to Japan, and especially of the transformational impact Zolgensma will have on the children and families affected by SMA,” said Dave Lennon, president, AveXis.

In May 2019, the U.S. Food and Drug Administration (FDA) approved Zolgensma for the treatment of pediatric patients less than two years of age with SMA with bi-allelic mutations in the *SMN1* gene. Approximately 400 patients have been treated with Zolgensma, including clinical trials, commercially and through the managed access program in the U.S. In the U.S. nearly all on-label patients have been approved by their payer for access to Zolgensma. AveXis is pursuing registration in close to three dozen countries with a Committee for Medicinal Products for Human Use opinion expected in 1Q 2020 and regulatory decisions anticipated in Switzerland, Canada and Australia in late 2020 or early 2021.

About Spinal Muscular Atrophy
SMA is the leading genetic cause of infant death and is designated as an intractable disease in Japan.[1] 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.[2] Approximately 60% of all SMA is Type 1. Approximately 15-20 SMA patients in Japan are expected to be eligible for treatment each year.[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.[3] 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.[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.[7] More than 30% of patients with SMA Type 2 will die by age 25.[8]

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 represents the first approved

therapeutic in the company's proprietary platform to treat rare, monogenic diseases using gene therapy. Approximately 400 patients have been treated with Zolgensma, including clinical trials, commercially and through the managed access program in the U.S.

AveXis 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 Genethon 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.

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," "may," "expected," "pending," "anticipate," "pipeline," "should," or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for Zolgensma, or regarding potential future revenues from Zolgensma. 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 Zolgensma, 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 Zolgensma will be commercially successful in the future. In particular, our expectations regarding Zolgensma 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 and economic conditions, including the effects of and efforts to mitigate pandemic disease 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 AveXis

AveXis, a Novartis company, is the world's leading gene therapy company, redefining the possibilities for patients and families affected by life-threatening genetic diseases through our innovative gene therapy platform. Founded in 2013 and headquartered in Bannockburn, IL, the goal of AveXis' cutting-edge science is to address the underlying, genetic root cause of diseases. AveXis pioneered foundational research, establishing AAV9 as an ideal vector for gene transfer in diseases affecting the central nervous system, laying the groundwork to build a best-in-class, transformational gene therapy pipeline. AveXis received its first U.S. Food and Drug Administration approval in May 2019 for the treatment of spinal muscular atrophy (SMA). AveXis is also developing therapies for other genetic diseases, including Rett syndrome, a genetic form of amyotrophic lateral sclerosis (ALS) *SOD1* and Friedreich's ataxia. For additional information, please visit www.avexis.com.

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 145 nationalities work at Novartis around the world. Find out more at https://www.novartis.com.

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