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AveXis receives positive CHMP opinion for Zolgensma®, the only gene therapy for spinal muscular atrophy (SMA)

- *Zolgensma® (onasemnogene abeparvovec), a one-time administered gene therapy, has been recommended for European Commission (EC) conditional approval for patients with spinal muscular atrophy (SMA) and a clinical diagnosis of Type 1 or SMA patients with up to three copies of the SMN2 gene*

- *Zolgensma has demonstrated significant and clinically meaningful therapeutic benefit in presymptomatic 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 5 years post-dosing*

- *In Europe, SMA is a significant burden to the healthcare system with cumulative estimated healthcare costs per child ranging between €2.5 to €4 million within the first 10 years alone*[1]

- *To support the urgent need to treat SMA as early as possible, AveXis is offering an innovative "Day One" access program to EU governments and reimbursement agencies to enable immediate access at time of EMA approval expected by June 2020*

Basel, March 27, 2020 – AveXis, a Novartis company, today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has adopted a positive opinion recommending conditional marketing authorization of Zolgensma® (onasemnogene abeparvovec) for the treatment of patients with 5q spinal muscular atrophy (SMA) with a bi-allelic mutation in the *SMN1* gene and a clinical diagnosis of SMA Type 1; or for patients with 5q SMA with a bi-allelic mutation in the *SMN1* gene and up to three copies of the *SMN2* gene. 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.[2,3] 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. The positive opinion is an important step towards offering a new treatment option in Europe for babies and young children with SMA.

The European Commission (EC) reviews the CHMP recommendation and usually delivers its final decision in approximately two months. The decision will be applicable to all 27 European Union member states, as well as Iceland, Norway, Liechtenstein and the United Kingdom.

"Today's positive CHMP opinion for Zolgensma marks a critical step closer to EC approval and to bringing the only gene therapy for SMA to Europe, helping to address the devastating impact the disease has on patients and their families," said Dave Lennon, president of AveXis.

“Zolgensma provides a transformational new way to treat this rare but debilitating disease – delivering a potentially life-saving medicine with a one-time administered treatment. Given the urgency to treat SMA and the novel nature of gene therapy, we need to be equally innovative in advancing access, so we are offering governments and reimbursement bodies a ‘Day One’ access program to enable rapid access to Zolgensma upon approval.”

“In the most severe forms of the disease, children who are not treated are unable to lift their heads, sit, stand, or even swallow, and typically do not survive beyond two years of age unless permanently ventilated,” said Dr. Francesco Muntoni, Professor and Pediatric Neurologist at Great Ormond Street Hospital for Children, London. “The results we have seen for Zolgensma to date from the STR1VE clinical trial show an impressive survival rate at the conclusion of the study, with the majority of patients being able to sit without support. And through follow-up on the START trial, an average of 4.5 years later, we can see the long-term potential this significant gene therapy may have for children with this rare disease.”

The CHMP positive opinion is based on the completed Phase 3 STR1VE-US and Phase 1 START trials that evaluated 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. STR1VE-EU, a comparable Phase 3 study is ongoing. Zolgensma demonstrated prolonged event-free survival; rapid motor function improvement, often within one month of dosing; and, sustained milestone achievement, including the ability to sit without support, a milestone never achieved in untreated Type 1 patients.[4]

Additional supportive data included 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 presymptomatic patients (<6 weeks at age of dosing) genetically defined by bi-allelic deletion of *SMN1* with 2 or 3 copies of *SMN2*. These data demonstrate rapid, age-appropriate major milestone gain, reinforcing the critical importance of early intervention in SMA patients.[4]

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.[4]

“We are delighted to know that EMA considers a new treatment effective to fight SMA and that it can benefit a part of our community. We rely on all relevant stakeholders, to work at their best to get it to patients without any delay. SMA Europe will continue working to ensure that all patients living with SMA in Europe have the possibility to access any treatment that can be beneficial for them in a timely and sustainable way,” said Mencía de Lemus, President of SMA Europe.

Zolgensma “Day One” access program

SMA is a significant burden to the healthcare system in Europe with cumulative estimated healthcare costs per child ranging between €2.5 to €4 million within the first 10 years alone.[1] Designed to work within existing pricing and reimbursement frameworks, yet recognizing the novel nature of a one-time gene therapy for a devastating and progressive disease, the “Day One” access program offers ministries of health and reimbursement bodies (in countries without pre-existing early access pathways) a variety of flexible options that can be implemented immediately at time of approval. The program is designed to ensure that the cost of patients treated before national pricing and reimbursement agreements are in place, are aligned with the value-based prices negotiated following clinical and economic assessments. The program is meant to ensure the continued integrity of the local pricing and reimbursement framework. AveXis is already in advanced discussions with multiple countries in Europe to agree on terms of the program. The following options can be customized for each country:

- Retroactive rebates ensuring early access costs are aligned with negotiated prices following local clinical and economic assessment processes
- Deferred payments and installment options allowing reimbursement bodies to manage budget impact during the early access phase
- Outcomes-based rebates negotiated following clinical and economic assessments can be applied to patients treated during the early access period
- Robust training for treating institutions on administration and follow-up care
- Access to RESTORE, a global SMA registry of patients who have been diagnosed with SMA that draws upon existing country registries

About Spinal Muscular Atrophy
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.[5] In Europe each year, approximately 550–600 infants are born with SMA.[6,7] 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.[8] 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.[9] More than 30% of patients with SMA Type 2 will die by age 25.[10]

Novartis will conduct a conference call with investors to discuss this news release on Monday, March 30, 2020 at 3 p.m. Central European Time and 9 a.m. Eastern Time. A simultaneous webcast of the call for investors and other interested parties may be accessed by visiting the Novartis website. A replay will be available after the live webcast by visiting https://www.novartis.com/investors/event-calendar.

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.[6] Approximately 400 patients have been treated with Zolgensma, including clinical trials, commercially and through the managed access program in the U.S. AveXis is pursuing registration in close to three dozen countries with regulatory decisions anticipated in Switzerland, Canada and Australia in late 2020 or early 2021.[6]

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.

In May 2019, the U.S. Food and Drug Administration approved Zolgensma for the treatment of pediatric patients less than two years of age with SMA with bi-allelic mutations in the *SMN1* gene. [11] In the U.S. nearly all on-label patients have been approved by their payer for access to Zolgensma. On March 19, 2020, Zolgensma was approved by Japanese Ministry of Health, Labour and Welfare (MHLW) for the treatment of SMA in patients under the age of two, including those who are pre-symptomatic at diagnosis. Reimbursement with MHLW is expected by the end of 1H20, pending agreement Zolgensma will be available at that time.

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 “positive CHMP opinion,” “offering,” “recommending,” “step towards,” “step closer,” “potential,” “can,” “will,” “plan,” “may,” “could,” “would,” “expect,” “anticipate,” “pipeline,” 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, 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 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 www.novartis.com.

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