**Novartis International AG**
**Novartis Global Communications**
CH-4002 Basel
Switzerland

https://www.novartis.com
https://twitter.com/novartisnews

## MEDIA & INVESTOR RELEASE

# AveXis receives EC approval and activates "Day One" access program for Zolgensma®, the only gene therapy for spinal muscular atrophy (SMA)

- *Zolgensma® (onasemnogene abeparvovec) is conditionally approved in Europe for the treatment of patients with spinal muscular atrophy (SMA) and a clinical diagnosis of SMA Type 1; or SMA patients with up to three copies of the SMN2 gene*

- *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 5 years post-dosing*

- *Immediate access to Zolgensma, aligned to the label, is available in France through the ATU framework and expected shortly in Germany*

- *AveXis in discussions with EU governments and reimbursement agencies to agree on terms of innovative "Day One" access program to enable rapid access in all EU countries given urgent need to treat SMA*

**Basel, May 19, 2020 –** AveXis, a Novartis company, today announced the European Commission (EC) granted conditional approval for 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. The approval covers babies and young children with SMA up to 21 kg according to the approved dosing guidance.

In Europe each year, approximately 550–600 infants are born with SMA, 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.[1,2,3] 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. Administered during a single, intravenous (IV) infusion, Zolgensma delivers a new working copy of the *SMN1* gene into a patient's cells, halting disease progression. According to Pediatric Neuromuscular Clinical Research (PNCR) natural history study of SMA, almost all patients under the age of five years of age will be under 21kg with some patients at 6, 7 or 8 weighing below 21 kg.[4] AveXis is planning a product presentation that allows for treatment of patients weighing up to 21 kg and is working with the European Medicines Agency (EMA) to finalize supply timelines.

“The EC approval of Zolgensma is a significant milestone for the SMA community, and further underscores the substantial clinical value of the only gene therapy for SMA, bringing new hope to those impacted by this rare, but devastating disease.” said Dave Lennon, president of AveXis. “Even under the current pandemic conditions, the urgent need to treat SMA has resulted in access pathways in France and Germany for Zolgensma, a potentially life-saving medicine delivered in a single dose. Additionally, we have met with more than 100 stakeholder organizations across Europe to discuss our “Day One” access program to enable rapid access with customizable options designed to work within local pricing and reimbursement frameworks.”

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.[5] Zolgensma is a transformative and highly innovative one-time gene therapy for a devastating and progressive genetic disease and is consistently priced worldwide under a value-based framework, however final pricing and reimbursement decisions are determined at the local level. Designed to work within existing, local pricing and reimbursement frameworks, the “Day One” access program offers ministries of health and reimbursement bodies a variety of flexible options that can be implemented immediately to support swift access and broad reimbursement.

The “Day One” access program ensures the cost of patients treated before national pricing and reimbursement agreements are in place align with the value-based prices negotiated following clinical and economic assessments. The program maintains the integrity of the local pricing and reimbursement frameworks with a variety of customizable options including:

- 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 registry of patients who have been diagnosed with SMA that draws upon existing country registries

Immediate access to Zolgensma, aligned to the label, is available in France through the ATU framework and expected shortly in Germany.

“Today’s approval brings tangible progress in harnessing the transformational power of gene therapy,” said Dr. Eugenio Mercuri, Professor, Pediatric Neurology, Catholic University, Rome, Italy. “The approval of Zolgensma represents an important new way for physicians to treat patients with SMA. 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 achieving functional milestones, like sitting without support, that wouldn't have been reached in untreated infants.”

“SMA Europe receives with deep excitement the news on the approval by the European Commission, of a gene therapy for treating a part of our community,” said Mencía de Lemus, President of SMA Europe. “Many hopes have been put into this much awaited therapy. It will be now be up to all stakeholders involved to ensure that treating doctors, together with parents, can take the best therapeutic option based on the benefit that each of them can provide to each individual. Gathering more data on how Zolgensma impacts in the lives of patients will be extremely important to better understand the potential of this new therapy on improving lives of those living with SMA.”

The EC approval 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, crawl and walk independently – milestones never achieved in untreated Type 1 patients.[6]

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 pre-symptomatic 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.[5]

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.[6] There is limited experience in patients 2 years of age and older or with body weight above 13.5 kg. The safety and efficacy of Zolgensma in these patients have not been established.

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 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.[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.[7,8] SMA is a rare, genetic neuromuscular disease caused by a lack of a functional *SMN1* gene, resulting in the progressive 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.[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 maximize functional abilities.[10] More than 30% of patients with SMA Type 2 will die by age 25.[11]

**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.[1] More than 500 patients have been treated with Zolgensma, including clinical trials, commercially and through the managed access program. AveXis is pursuing registration in close to three dozen countries with regulatory decisions anticipated in Switzerland, Canada, Australia, Argentina, South Korea and Brazil in late 2020 or early 2021.[1]

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.[12] 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.[13] Today's EC approval applies to all 27 European Union member states, as well as Iceland, Norway, Liechtenstein and the United Kingdom.

**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 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.

Novartis is on Twitter. Sign up to follow @Novartis at **https://twitter.com/novartisnews**
For Novartis multimedia content, please visit **https://www.novartis.com/news/media-library**
For questions about the site or required registration, please contact media.relations@novartis.com.

**References**


1. Data on file.
2. Anderton RS and Mastaglia FL. *Expert Rev Neurother*. 2015;15(8):895-908.
3. National Organization for Rare Disorders (NORD). Spinal Muscular Atrophy. http://rarediseases.org/rarediseases/spinal-muscular-atrophy/. Accessed October 9, 2018
4. PNCR, Pediatric Neuromuscular Clinical Research. PNCR Database: Weights (kg) by Patient Ages (Months) for SMA Types I, II, and III All Visits. Accessed March 13, 2020. WHO, World Health Organization. Growth reference 5-19 years. Weight-for-age (5-10 years). Accessed March 29, 20.
5. Estim. 10-year cumulative SMA costs for major EU markets based on available data including local healthcare resource utilizations studies, local databases and public information from previous SMA therapy economic assessments, as of February 21, 2020.
6. STR1VE-US, START and SPR1NT clinical data on file.
7. Finkel RS, et al. *Neurology*. 2014;83(9):810-817.
8. Verhaart IEC, et al. *J Neurol*. 2017;264(7):1465-1473.
9. Soler-Botija C, et al. *Brain*. 2002;125(7):1624-1634.
10. Wang CH, et al. J Child Neurol. 2007;22(8):1027-1049.
11. Darras BT, Finkel RS Spinal Muscular Atrophy. Chapter 25 - Natural History of Spinal Muscular Atrophy. October 2017.
12. U.S. FDA approval of Zolgensma: https://www.fda.gov/vaccines-blood-biologics/zolgensma.
13. Japanese MHLW approval of Zolgensma: https://www.novartis.com/news/media-releases/novartis-receives-approval-from-japanese-ministry-health-labour-and-welfare-zolgensma-only-gene-therapy-patients-spinal-muscular-atrophy-sma.


# # #


**Novartis Media Relations**
Central media line: +41 61 324 2200
E-mail: media.relations@novartis.com

Anja von Treskow
Novartis Global External Communications
+41 61 79 392 8697(mobile)
Anja.von_treskow@novartis.com

Farah Bulsara Speer
SVP, Corporate Communications, AveXis
+1 312 543 2881 (mobile)
fSpeer259@avexis.net

Eric Althoff
Novartis External Communications
+1 646 438 4335 (mobile)
eric.althoff@novartis.com

**Novartis Investor Relations**
Central investor relations line: +41 61 324 7944
E-mail: investor.relations@novartis.com

| Central | | North America | |
|---|---|---|---|
| Samir Shah | +41 61 324 7944 | Sloan Simpson | +1 862 778 5052 |
| Pierre-Michel Bringer | +41 61 324 1065 | Cory Twining | +1 862 778 3258 |
| Thomas Hungerbuehler | +41 61 324 8425 | | |
| Isabella Zinck | +41 61 324 7188 | | |