New AveXis data at AAN showed long-term durability of Zolgensma® in patients with spinal muscular atrophy (SMA) Type 1

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- - Interim long-term follow-up data showed all enrolled Cohort 2 patients maintained motor function and milestones achieved during the Phase 1 START trial
- - Mean age of follow-up since dosing with Zolgensma (onasemnogene abeparvovec-xioi; AVXS-101) was nearly four years, with some patients nearing five years of age
- - No loss of milestones or waning of effect in long-term follow-up of START adds to evidence of long-term durability of Zolgensma

BASEL, Switzerland, May 7, 2019 /PRNewswire/ -- AveXis, a Novartis company, today announced interim long-term follow-up data from the Phase 1 START trial of the investigational product Zolgensma® (onasemnogene abeparvovec-xioi; AVXS-101)[1] that showed durability of the gene therapy in patients with spinal muscular atrophy (SMA) Type 1 nearly four years after treatment. These data were presented during the 2019 American Academy of Neurology (AAN) Annual Meeting.

"As someone who has worked with SMA Type 1 patients for more than five decades and witnessed the devastation the disease has on families, it is truly remarkable to now be able to watch these babies grow up and become children living functional lives," said Jerry Mendell, M.D., Center for Gene Therapy at Nationwide Children's Hospital. "At the time we began the START study, most babies with SMA Type 1 would die or require permanent ventilation before age two. Now with four years of data, we are seeing clear evidence of the potential of gene therapy to effectively, over several years, halt motor neuron loss and alter the course of SMA Type 1 with a single dose."

The Phase 1 START study evaluated the safety and efficacy of intravenous (IV) Zolgensma in SMA Type 1 patients with the onset of clinical symptoms before six months of age. At the 24-month study closeout, all 12 patients in the therapeutic dose cohort were alive and free of permanent ventilation as opposed to only 8 percent of patients expected to reach this achievement in natural history. The most commonly observed side effect in the START clinical trial was elevated liver enzymes. Among patients receiving the proposed therapeutic dose (Cohort 2), 11/12 patients (91.7 percent) were able to hold their head erect for ≥ three seconds and sit without support for ≥ five seconds, 10 patients (83.3 percent) were able to sit without support for ≥ 10 seconds, nine patients (75.0 percent) were able to sit without support for ≥ 30 seconds, and two patients each (16.7 percent) were able to stand alone, walk with assistance and walk alone.

START Long-Term Follow-Up Data in Cohort 2 Patients as of March 8, 2019
A total of 10 of the 12 patients in Cohort 2 voluntarily enrolled in an ongoing observational long-term follow-up of the START trial. All patients (n=10) were alive and event-free. An event is defined as either death or at least 16 hours per day of required ventilation support for breathing for 14 consecutive days in the absence of acute reversible illness or perioperative change.

The mean time since treatment was 3.7 years, with a range of 3.3 to 4.3 years. The mean age at last follow-up was 3.9 years, with a range of 3.4 to 4.8 years.

As of March 8, 2019, all patients maintained the motor function and milestones gained during the trial following treatment with Zolgensma. In addition, no patients had any additional requirements for ventilatory or nutritional support.

Two of the four patients who required Bilevel Positive Airway Pressure (BiPAP) support at the beginning of the long-term follow-up study no longer required it regularly.

No new treatment-related adverse events have emerged during the follow-up period.

Patients in START were treated with gene therapy alone during the 24-month study duration. In the long-term follow-up study, 7 of 10 (70.0 percent) patients remained on monotherapy alone. Initiation of combination therapy was at parental and physician discretion and was not due to loss of motor function.

The sustained clinical impact following dosing suggests that Zolgensma effectively halts motor neuron loss and adds to the evidence of the long-term durability of Zolgensma.

About Zolgensma®

Zolgensma® (onasemnogene abeparvovec-xioi; AVXS-101) is an investigational gene therapy currently in development as a one-time infusion for SMA Type 1. Zolgensma is designed to address the genetic root cause of SMA and prevent further muscle degeneration by providing a functional copy of the human SMN gene to halt disease progression through sustained SMN protein expression. Zolgensma represents the first in a proprietary platform to treat rare, monogenic diseases using gene therapy. Zolgensma was developed in partnership with Genethon. In December 2018, the FDA accepted the company's Biologics License Application for use of Zolgensma with SMA Type 1 patients. The drug previously received Breakthrough Therapy designation and has been granted Priority Review by the FDA, with regulatory action anticipated in May 2019. In addition, the drug is anticipated to receive approval in Japan and the European Union later this year.

About Spinal Muscular Atrophy (SMA)

SMA is a severe neuromuscular disease characterized by the loss of motor neurons leading to progressive muscle weakness and paralysis. SMA is caused by a genetic defect in the SMN1 gene that codes SMN, a protein necessary for survival of motor neurons. The incidence of SMA is approximately one in 10,000 live births and is the leading genetic cause of infant mortality. The most severe form of SMA is Type 1, a lethal genetic disorder characterized by rapid motor neuron loss and associated muscle deterioration, which results in mortality or the need for permanent ventilation support by 24 months of age for more than 90 percent of patients.

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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 and economic conditions; safety, quality 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 dedicated to developing and commercializing novel treatments for patients suffering from rare and life-threatening neurological genetic diseases. Our initial product candidate, Zolgensma, is a proprietary gene therapy currently in development for the treatment of spinal muscular atrophy, or SMA. In addition to developing Zolgensma to treat SMA, AveXis also plans to develop other novel treatments for rare neurological diseases, including Rett syndrome and a genetic form of amyotrophic lateral sclerosis caused by mutations in the superoxide dismutase 1 (SOD1) gene. 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 more than 750 million people globally and we are finding innovative ways to expand access to our latest treatments. About 105 000 people of more than 140 nationalities work at Novartis around the world. Find out more at www.novartis.com.

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References

1. The brand name Zolgensma® (onasemnogene abeparvovec-xioi) has been provisionally approved by the FDA for the investigational product AVXS-101, but the product itself has not received marketing authorization or BLA approval from any regulatory authorities.

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