AveXis Announces Innovative Zolgensma® Gene Therapy Access Programs for US Payers and Families

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- - One-time treatment with Zolgensma (onasemnogene abeparvovec-xioi) is designed to replace lifetime of chronic therapy for all pediatric patients with SMA
- - Annualized cost of Zolgensma is USD 425,000 per year for 5 years: 50% less than multiple established value-based pricing benchmarks including the 10-year current cost of chronic SMA therapy(1)
- - AveXis is working closely with payers to create 5-year outcomes-based agreements and novel pay-over-time options; Time is Neurons program to support rapid SMA treatment post-diagnosis
- - Comprehensive OneGene Program™ provides dedicated, personalized support for Zolgensma patients

BASEL, Switzerland, May 24, 2019 /PRNewswire/ -- AveXis, a Novartis company, today announced innovative access programs for Zolgensma® (onasemnogene abeparvovec-xioi) for the treatment of pediatric patients less than 2 years of age with spinal muscular atrophy (SMA) with bi-allelic mutations in the survival motor neuron 1 (SMN1) gene. AveXis is working closely with payers to offer pay-over-time options up to 5 years and outcomes-based agreements up to 5 years, as well as providing a patient program to support affordability and access.

"Zolgensma is a historic advance for the treatment of SMA and a landmark one-time gene therapy. Our goal is to ensure broad patient access to this transformational medicine and to share value with the healthcare system," said Vas Narasimhan, CEO of Novartis. "We have used value based pricing frameworks to price Zolgensma at around 50% less than multiple established benchmarks including the 10-year current cost of chronic SMA therapy. In addition, the price of Zolgensma is expected to be within the range of traditional cost-effectiveness thresholds used by ICER when updated for its full labeled indications. We believe by taking this responsible approach, we will help patients benefit from this transformative medical innovation and generate significant cost savings for the system over time."

"Innovative science like Zolgensma required us to be equally innovative in offering customized access solutions to meet the many needs of payers and patients," said Dave Lennon, president of AveXis. "We are partnering to accelerate coverage decisions with both government and commercial payers. We are offering a pay-over-time model for this one-time treatment to accommodate the current structure of the US healthcare system and we have also established outcomes-based agreements with payers because we believe in the long-term value of Zolgensma and are willing to stand behind the therapy."

The current 10-year cost of chronic therapy, which is given over the patient's lifetime, can often exceed USD 4 million in just the first 10 years of a young child's life.[1] In addition, that therapy stops working if treatment is stopped.[2] Zolgensma is expected to save costs in the healthcare system compared to chronic treatment for the treatment and care of SMA.[3] The wholesale acquisition cost of Zolgensma of USD 2.125 million is:

- 50% of the 10-year cost of current chronic SMA treatment (estimated at USD 4.1 million)[1]
- 50% below 10-year treatment costs for genetic pediatric ultra-rare diseases (estimated at USD 4.4 million to USD 5.7 million)[4*]
- 50% below the ICER ultra-rare disease cost-effectiveness threshold; Zolgensma pricing places it at approximately USD 250,000 per quality-adjusted life-year (QALY)[5]

"We are at the forefront of an exciting time in healthcare when we'll be able to see major advancements in medical care with potentially curative gene therapies. While there are many questions that we as a healthcare system need to consider, what does not change is our work to ensure that these life-saving medications are affordable and available to the patients that need them," said Steve Miller, M.D., chief clinical officer, Cigna Corporation. "We look forward to continuing the work we have started with AveXis to find unique solutions like installment payments and outcomes-based agreements for these life changing gene therapies."

AveXis has partnered with Accredo® to offer a pay-over-time option of up to 5 years to help ease possible short-term budget constraints, especially for states, small payers and self-insured employers. In addition, CuraScript SD® has been selected as the sole specialty distributor given its rare disease experience, including gene and cell therapies.

Reflecting the pioneering nature of these programs, more than 15 payers are in advanced discussions of terms with AveXis, with some having already agreed, in principle, to terms.

"We are thrilled to be able to offer our members access to this groundbreaking gene therapy, particularly in light of AveXis agreeing to place a portion of the cost at risk, contingent upon demonstrating continued performance over a five-year period," said Michael Sherman, M.D., M.B.A., chief medical officer of Harvard Pilgrim Health Care. "The clinical benefits of gene therapy for infants with life-threatening genetic diseases, such as SMA, are undeniable, and our innovative, outcomes-based agreement helps ensure that we balance access and affordability for our members. While we anticipate that Harvard Pilgrim would see a small number of newly-diagnosed patients with the very rare SMA Type 1 each year, we believe it is our responsibility to provide access to this lifesaving treatment."

OneGene Program™ to support patients and families along their treatment journey with Zolgensma
AveXis patient support program, called OneGene Program™, is a comprehensive, individualized support program that provides a dedicated, personalized support team focused on the needs of each family throughout the Zolgensma treatment journey. This includes answering questions about Zolgensma, verifying reimbursement assistance and coordinating financial assistance programs for eligible patients. For more information, caregivers and healthcare professionals can call 1-855-441-GENE (1-855-441-4363).

Time is Neurons education program for commercial payers and state Medicaid programs to support rapid treatment
Lost motor neurons are irreplaceable, which means early diagnosis and treatment are critical.[6,7] Through its Time is Neurons education effort, AveXis has been working closely with payers to highlight the importance of early treatment. AveXis is delivering on the urgent need to treat pediatric patients with SMA with the goal of reduced prior authorization turnaround time, allowing them ideally to be treated within 2 weeks of diagnosis.

AveXis paves path to make the therapy available to children around the world via expanded manufacturing and paid managed access plan
AveXis plans to make Zolgensma available to patients affected by SMA globally, and simultaneous priority registration filings started in 2018 in the US, Europe and Japan. Preparations are underway to file for registration in other countries. In the interim, AveXis has arranged to make the product available for international markets, subject to local laws and regulations, as a part of its paid Managed Access Program via a collaboration with Durbin, a third-party provider. International inquiries regarding availability of Zolgensma outside of the US may be made by contacting Durbin at AveXisMAP@DurbinGlobal.com or +44 20 8869 6506.

AveXis' ongoing commitment to research and development for the treatment of rare genetic diseases
AveXis has four new programs entering clinical trials in 2019 and 2020, including for Rett syndrome and a genetic form of ALS, also known as Lou Gehrig's disease. Manufacturing a gene therapy is a difficult and complicated process and AveXis is paving the way for the industry with leading talent and gene therapy manufacturing expertise. AveXis has approximately 1 million square-feet of manufacturing space across four sites – the most potential capacity of any gene therapy company – and plans to have 1,000 employees in highly-skilled manufacturing roles by the end of 2019.

About Zolgensma Clinical Data
The efficacy of Zolgensma in pediatric patients less than 2 years of age with SMA with bi-allelic mutations in the SMN1 gene was evaluated in STR1VE, an open-label, single-arm clinical trial (ongoing), and in START, an open-label, single-arm, ascending-dose clinical trial (completed). Patients experienced onset of clinical symptoms consistent with SMA before 6 months of age. All patients had genetically confirmed bi-allelic SMN1 gene deletions, 2 copies of the SMN2 gene, and absence of the c.859G>C modification in exon 7 of SMN2 gene (which predicts a milder phenotype). All patients had baseline anti-AAV9 antibody titers of ≤ 1:50, measured by ELISA. In both trials, Zolgensma was delivered as a single-dose intravenous infusion.

Efficacy was established on the basis of survival, and achievement of developmental motor milestones such as sitting without support. Survival was defined as time from birth to either death or permanent ventilation. Permanent ventilation was defined as requiring invasive ventilation (tracheostomy), or respiratory assistance for 16 or more hours per day (including

noninvasive ventilatory support) continuously for 14 or more days in the absence of an acute reversible illness, excluding perioperative ventilation. Efficacy was also supported by assessments of ventilator use, nutritional support and scores on the Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND). CHOP-INTEND is an assessment of motor skills in patients with infantile-onset SMA.

The ongoing clinical trial, STR1VE, enrolled 21 patients (10 male and 11 female) with infantile-onset SMA. Before treatment with Zolgensma, none of the 21 patients required non-invasive ventilator (NIV) support, and all patients could exclusively feed orally (i.e., no need for non-oral nutrition). The mean CHOP-INTEND score at baseline was 31.0 (range 18 to 47). All the patients received 1.1×10^{14} vg/kg of Zolgensma. The mean age of the 21 patients at the time of treatment was 3.9 months (range 0.5 to 5.9 months).

As of the March 2019 data cutoff, 19 patients were alive without permanent ventilation (i.e., event-free survival) and were continuing in the trial, while one patient died at age 7.8 months due to disease progression, and one patient withdrew from the study at age 11.9 months. The 19 surviving patients who were continuing in the trial ranged in age from 9.4 to 18.5 months. By the data cutoff, 13 of the 19 patients continuing in the trial reached 14 months of age without permanent ventilation, one of the study's co-primary efficacy endpoints. In addition to survival, assessment of the other co-primary efficacy endpoint found that 10 of the 21 patients (47.6%) achieved the ability to sit without support for ≥ 30 seconds between 9.2 and 16.9 months of age (mean age was 12.1 months). Based on the natural history of the disease, patients who met the study entry criteria would not be expected to attain the ability to sit without support, and only approximately 25% of these patients would be expected to survive (i.e., being alive without permanent ventilation) beyond 14 months of age. In addition, 16 of the 19 patients had not required daily NIV use.

Comparison of the results of the ongoing clinical trial to available natural history data of patients with infantile-onset SMA provides primary evidence of the effectiveness of Zolgensma.

The completed clinical trial, START, enrolled 15 patients (6 male and 9 female) with infantile-onset SMA, 3 in a low-dose cohort and 12 in a high-dose cohort. At the time of treatment, the mean age of patients in the low-dose cohort was 6.3 months (range 5.9 to 7.2 months), and 3.4 months (range 0.9 to 7.9 months) in the high-dose cohort. The dosage received by patients in the low-dose cohort was approximately one-third of the dosage received by patients in the high-dose cohort. However, the precise dosages of Zolgensma received by patients in this completed clinical trial are unclear due to a change in the method of measuring Zolgensma concentration, and to decreases in the concentration of stored Zolgensma over time. The retrospectively-estimated dosage range in the high-dose cohort is approximately 1.1×10^{14} to 1.4×10^{14} vg/kg.

By 24 months following Zolgensma infusion, one patient in the low-dose cohort met the endpoint of permanent ventilation; all 12 patients in the high-dose cohort were alive without permanent ventilation. None of the patients in the low-dose cohort were able to sit without support, or to stand or walk; in the high-dose cohort, 9 of the 12 patients (75.0%) were able to sit without support for ≥ 30 seconds, and 2 patients (16.7%) were able to stand and walk without assistance. Comparison of the results of the low-dose cohort to the results of the high-dose cohort shows a dose-response relationship that supports the effectiveness of Zolgensma.

About Zolgensma® (onasemnogene abeparvovec-xioi)
Zolgensma (onasemnogene abeparvovec-xioi) is a proprietary gene therapy approved by the US Food and Drug Administration for the treatment of pediatric patients less than 2years of age with spinal muscular atrophy (SMA) with bi-allelic mutations in the survival motor neuron 1 (SMN1) gene. 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 intravenous (IV) infusion. Zolgensma represents the first approved therapeutic in a proprietary platform to treat rare, monogenic diseases using gene therapy. The therapy is also 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.[8,9] The incidence of SMA is approximately 1 in 10,000 live births and it is the leading genetic cause of infant mortality.[9,10] The most severe form of SMA is Type 1, a lethal genetic disorder characterized by rapid motor neuron loss and associated muscle deterioration, resulting in mortality or the need for permanent ventilation support by 24

months of age for more than 90 percent of patients if left untreated.[11]

Indication
Zolgensma (onasemnogene abeparvovec-xioi) is an adeno-associated virus vector-based gene therapy indicated for the treatment of pediatric patient less than 2 years of age with spinal muscular atrophy (SMA) with bi-allelic mutations in the survival motor neuron 1 (SMN1) gene.

Limitation of Use:

The safety and effectiveness of repeat administration of Zolgensma have not been evaluated.

The use of Zolgensma in patients with advanced SMA (e.g., complete paralysis of limbs, permanent ventilator-dependence) has not been evaluated.

Important Safety Information

Acute Serious Liver Injury
Acute serious liver injury and elevated aminotransferases can occur with Zolgensma. Patients with pre-existing liver impairment may be at higher risk. Prior to infusion, assess liver function of all patients by clinical examination and laboratory testing (e.g., hepatic aminotransferases [aspartate aminotransferase and alanine aminotransferase], total bilirubin and prothrombin time). Administer systemic corticosteroid to all patients before and after Zolgensma infusion. Continue to monitor liver function for at least 3 months after infusion.

Thrombocytopenia
Transient decreases in platelet counts, some of which met the criteria for thrombocytopenia, were observed at different time points after Zolgensma infusion. Monitor platelet counts before Zolgensma infusion and on a regular basis afterwards.

Elevated Troponin-I
Transient increases in cardiac troponin-I levels (up to 0.176 mcg/L) were observed following Zolgensma infusion in clinical trials. The clinical importance of these findings is not known. However, cardiac toxicity was observed in animal studies. Monitor troponin-I before Zolgensma infusion and on a regular basis for at least 3 months afterwards.

Adverse Reactions
The most commonly observed adverse reactions (incidence ≥5%) were elevated aminotransferases and vomiting.

Please read full Prescribing Information for Zolgensma, including Boxed Warning for Acute Serious Liver Injury.

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 "designed to," "to create," "to support," "to offer," "goal," "to ensure," "to share value," "expected," "will," "partnering," "offering," "long-term," "can," "forefront," "exciting," "potentially," "look forward to," "advanced discussions," "priority registration filings," "underway," "commitment," "entering clinical trials," "paving the way," "potential," "plans," "anticipated," or similar terms, or by express or implied discussions regarding the acceptability of Zolgensma pricing and access programs, regarding potential marketing approvals, new indications or labeling for Zolgensma and the investigational products described in this press release, 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 Zolgensma pricing and access programs announced in this release will be accepted by the public, the government or by payers. Neither can there be any guaranty that Zolgensma or the investigational 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 could be affected by, among other things, global trends toward health care cost containment, including government, payer and general public pricing and reimbursement pressures, and requirements for increased pricing transparency; regulatory actions or delays or government regulation generally; general political and economic conditions; the uncertainties inherent in research and development, including

clinical trial results and additional analysis of existing clinical data; our ability to obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; 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, Zolgensma, is a proprietary gene therapy approved by the US Food and Drug administration for the treatment of pediatric patients with SMA less than 2 years of age with spinal muscular atrophy (SMA) with bi-allelic mutations in the survival motor neuron 1 (SMN1) gene. In addition to developing Zolgensma to treat all forms of 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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