



Novartis stands behind Zolgensma® (onasemnogene abeparvovec-xioi) for the treatment of children less than 2 years of age with spinal muscular atrophy

August 6, 2019

Basel, August 6, 2019 – Today the FDA released a statement addressing data integrity issues with the Biologics License Application (BLA) for Zolgensma® (onasemnogene abeparvovec-xioi). First and foremost, we are fully confident in the safety, quality and efficacy of Zolgensma. The FDA supports the continued marketing and use of Zolgensma for patients with spinal muscular atrophy (SMA) less than 2 years of age. We maintain that the totality of the evidence demonstrating the product's effectiveness and its safety profile continue to provide compelling evidence supporting an overall favorable benefit-risk profile. We remain steadfast that this important treatment remain available to pediatric patients with SMA less than 2 years of age.

On June 28th, AveXis voluntarily self-disclosed to the FDA and subsequently to other health authorities that some data previously submitted to the agency as part of our BLA package was inaccurate. AveXis had become aware of allegations of data manipulation in a specific animal testing procedure used in the development of the product. The assays in question were used for initial product testing and are not currently used for commercial product release. An investigation was immediately initiated to rapidly understand any implications and address the situation. Once we had interim conclusions from our investigations, we shared our findings with the FDA. As noted by the FDA, the data in question were a small portion of our overall submission and are limited to an older process no longer in use.

At no time during the investigation did the findings indicate issues with product safety, efficacy or quality. We remain fully capable of releasing high-quality, fully compliant Zolgensma to patients in need. We have and will continue to work in close cooperation with the FDA to appropriately update our submission and address any quality gaps identified. We are committed to ensuring the highest levels of transparency and integrity with health agencies, as well as with the patients and providers we serve. We do not expect this to impact the timing of our ongoing Zolgensma regulatory filings and development programs. AveXis is committed to taking appropriate action to prevent future incidents across its portfolio of development programs.

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 2 years 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. The incidence of SMA is approximately 1 in 10,000 live births and it 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, 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.

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 \geq 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 "stands behind," "confident," "supports," "supporting," "remain steadfast," "will," "committed," "expect," "ongoing," "anticipated," "later this year," "potential," "expectations," 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; 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 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 108,000 people of more than 140 nationalities work at Novartis around the world. Find out more at www.novartis.com.

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