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MEDIA RELEASE • MEDIA RELEASE • MEDIA RELEASE

AveXis presents AVXS-101 IT data demonstrating remarkable increases in HFMSE scores and a consistent clinically meaningful response in older patients with SMA Type 2

- *SMA Type 2 patients between two and five years of age who received Dose B met the primary efficacy endpoint with a remarkable mean increase of 6.0 points in HFMSE scores from baseline to month 12, twice the clinically meaningful threshold, as measured by a validated, widely utilized and highly accepted scale developed specifically for older patients with SMA*

- *Nearly all patients (92%) in this cohort achieved a clinically meaningful ≥3-point increase during the study period, demonstrating a consistent response following gene therapy*

- *Increases observed in HFMSE reflect the preservation of motor neurons connected to key muscle groups impacted in SMA Type 2, allowing for motor development such as trunk control when rolling and sitting, and transitioning from lying to sitting*

- *Adverse events observed in STRONG were consistent with the AVXS-101 IV program; no deaths were reported, and no new signals identified*

- *In response to the partial clinical hold on the AVXS-101 IT program by the FDA in October 2019, AveXis provided data indicating no clinical reports of sensory neuronopathy in 335 patients following IV or IT treatment with AVXS-101; FDA is expected to respond by Q2 2020*

Basel, March 24, 2020 – AveXis, a Novartis company, today announced that new data from the Phase 1/2 STRONG study demonstrated a one-time intrathecal (IT) administration of AVXS-101 in patients ≥2 years and <5 years old with spinal muscular atrophy (SMA) Type 2 who received Dose B (1.2×10^{14} vg) met the primary efficacy endpoint, achieving a remarkable mean increase from baseline of 6.0 points in the Hammersmith Functional Motor Scale-Expanded (HFMSE), twice the clinically meaningful threshold established in previous SMA studies and reflecting improvement in three to six skills. In addition, nearly all patients (92%) in this group achieved a clinically meaningful ≥3-point increase in HFMSE at any post-baseline visit during the study period, demonstrating a consistent response and a dramatic difference from the natural history control group (P <0.0001). Increases observed in HFMSE reflect the preservation of motor neurons connected to key muscle groups impacted in SMA Type 2, allowing for motor development such as trunk control when rolling and sitting, and transitioning from lying to sitting. In contrast to these findings, according to natural history, untreated SMA Type 2 patients typically experience a steady decline in motor function, and more than 30% die by age 25.[1] These data are being presented today during a virtual Clinical Trial Session conducted by the

Muscular Dystrophy Association (MDA), scheduled after the 2020 MDA Annual Conference was cancelled due to COVID-19.

“Nearly all patients evaluated on the gold standard Hammersmith scale achieved a clinically meaningful response, consistently demonstrating improved motor function through continuous, stable SMN protein expression,” said Dave Lennon, president of AveXis. “Among patients with SMA Type 2 between two and five years of age, STRONG data demonstrated potential best-in-category profile with remarkable motor function improvement following a single, one-time intrathecal dose. We look forward to sharing these data with regulators to further our discussions toward registration of intrathecal AVXS-101.”

HFMSE is a validated, widely utilized and highly accepted scale for assessing motor function, specifically designed for use in SMA patients ≥2 years of age. HFMSE is recognized by global regulatory agencies due to its ability to monitor change in a broad spectrum of weaker and stronger patients.

- A 3-point change on the HFMSE is agreed upon by experts to represent a clinically meaningful change involving two or three skills.
- A 6-point improvement reflects achievements in three to six skills. Patients in STRONG achieved a broad array of improvements in motor skills, such as trunk control when rolling and sitting and transitioning from lying to sitting. In non-ambulatory patients, improved strength and consolidation of critical functions allows for better maneuverability, transitioning and integration of proximal and distal functions that enable more advanced use of their well-developed fine motor skills. These improvements were seen even in patients who were very weak at baseline.

“As a result of evolving treatment options, older SMA Type 2 patients now expect to achieve meaningful improvements in motor function that enable them to perform important activities and set them on a path toward greater independence,” said Olga Santiago, M.D., Chief Medical Officer, AveXis. “Given the robust response, these STRONG data indicate AVXS-101 delivered intrathecally could potentially be a new one-time treatment option for patients and their clinicians.”

Phase 1/2 STRONG Data as of December 2, 2019

STRONG is an ongoing, open-label, multi-center trial designed to evaluate the efficacy, safety and tolerability of one-time intrathecal (IT) administration of AVXS-101 in SMA Type 2 patients who have three copies of the *SMN2* gene, and who are able to sit but unable to stand or walk at the time of study entry. Patients were divided into two groups based on age at time of treatment: patients who are ≥6 months but <2 years and patients who are ≥2 years but <5 years. As of the data cut-off, 32 patients were enrolled and have been treated with one of three doses: Dose A (6.0×10^{13} vg), Dose B (1.2×10^{14} vg) and Dose C (2.4×10^{14} vg).

In patients ≥2 years to <5 years old (n=12):

- The primary efficacy endpoint of change in HFMSE score from baseline was achieved (*P* <0.0021) compared to a natural history control group.
    - To ensure appropriate comparison, a natural history group was matched with the treatment group inclusion criteria using the Pediatric Neuromuscular Clinical Research Network (PNCR) database.
- Patients achieved clinically meaningful improvements in motor function, as demonstrated by 6.0-point increase from baseline in HFMSE scores at 12 months post-dosing.
- Nearly all (11/12) patients in this group achieved a clinically meaningful ≥3-point increase in HFMSE during the study period.
- Four motor milestones have been achieved among three patients in the Dose B group using Bayley-III, which is a scale created to assess normal development, including one patient who gained the ability to walk with assistance.
- The secondary efficacy endpoint of the ability to walk independently for ≥5 steps was not achieved by any patient.

In Dose B patients ≥6 months to <2 years old (n=13)

- The primary and secondary efficacy endpoints were the ability to stand without support for ≥3 seconds and walk independently for ≥5 steps, respectively.
    - 1 patient achieved the ability to stand alone and walk independently
- Five of the six (83%) patients who became old enough to be evaluated on the HFMSE achieved a 3.0-point increase from baseline at any time after 24 months of age, in-line with the older cohort.
- 18 motor milestones were achieved among six out of the 13 patients, including one patient who gained the ability to stand independently, and went on to walk alone.

Efficacy data from four patients currently enrolled in Dose C were not presented, and further enrollment has been suspended. In October 2019, the U.S. Food & Drug Administration (FDA) placed a partial hold on the AVXS-101 IT program following findings from a small, AveXis-initiated pre-clinical study in which animals treated with intrathecal AXVS-101 showed dorsal root ganglia mononuclear cell inflammation, sometimes accompanied by neuronal cell degeneration or loss. AveXis submitted a response to the FDA with further characterization and a commitment to further study these preclinical findings, along with a thorough analysis of clinical safety to date showing no clinical reports of sensory neuronopathy in 335 patients following treatment with AVXS-101 (intravenous and intrathecal administration) as of December 31, 2019. The FDA is expected to respond to the submission by Q2 2020.

Adverse events (AEs) observed in STRONG were consistent with the intravenous AVXS-101 program. No new clinical safety signals were detected in the study. Nearly all patients in STRONG study experienced at least one adverse event (AE) and 12 patients (38%) were reported to have an AE considered by the investigator to be related to treatment. Serious AEs were reported in 22% (n=7) of patients. A total of 13 serious AEs were reported in seven patients: pneumonia (n=2), influenza, bronchitis, rhinovirus infection, respiratory tract infection, elevated ALT, elevated AST, acute respiratory failure, asthma, respiratory failure (n=1 each), blood alkaline phosphatase increased (n=2). Many of these AEs (i.e. respiratory infections) are consistent with events experienced by children with SMA and the general population. Transaminitis events in two patients were considered probably related to treatment and resolved completely. There were no deaths reported.

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 AVXS-101 Intrathecal Administration
Investigational IT administration of AVXS-101 is being evaluated in SMA Type 2 patients in a Phase 1/2 clinical trial.

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] 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.[3]
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.[4] 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.[5] 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.[6] More than 30% of patients with SMA Type 2 will die by age 25.[1]

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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 www.novartis.com.

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