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MEDIA & INVESTOR RELEASE

Novartis intrathecal onasemnogene abeparvovec Phase III study meets primary endpoint in children and young adults with SMA

Ad hoc announcement pursuant to Art. 53 LR

- *The Phase III STEER study met its primary endpoint showing an increase from baseline in HFMSE total score in patients with SMA treated with intrathecal onasemnogene abeparvovec (OAV101 IT)*

- *OAV101 IT is the first investigational gene therapy to provide clinical benefit in treatment-naïve patients with SMA aged two and older with a positive risk benefit profile*

- *Novartis plans to share results with regulatory agencies in 2025 with the aim to make OAV101 IT available to help patients with SMA in need*

Basel, [December 30, 2024] – Novartis today announced positive topline results from the Phase III STEER study. This pivotal study assessed the efficacy and safety of investigational intrathecal onasemnogene abeparvovec (OAV101 IT) in treatment-naïve patients with spinal muscular atrophy (SMA) Type 2, aged two to less than 18 years who are able to sit but have never walked independently.[1] Efficacy and safety results for OAV101 IT were compared against a sham control, a procedure designed to mimic the administration of an investigational drug, without delivering any active treatment.

The STEER study met its primary endpoint showing an increase from baseline across the study population in total Hammersmith Functional Motor Scale - Expanded (HFMSE) scores. HFMSE is a gold standard for SMA-specific assessment of motor ability and disease progression.[2,3,4,5,6] The increase was observed in patients treated with OAV101 IT compared to sham controls indicating better motor function in patients with SMA.

The safety profile of OAV101 IT was favorable. The overall adverse events and serious adverse events were similar between arms. The most common adverse events were upper respiratory tract infection, pyrexia and vomiting.

Novartis plans to share results with regulatory agencies in 2025, including the US Food and Drug Administration (FDA), with the aim to make OAV101 IT available to help patients with SMA in need. Data will be presented at an upcoming medical meeting in 2025.

“Many patients with SMA currently rely on chronic treatments to manage their disease. These positive topline results from the STEER trial underscore the efficacy, safety and tolerability of

OAV101 IT in patients with SMA aged two and above," said Shreeram Aradhye, M.D., President, Development and Chief Medical Officer, Novartis. "The totality of evidence clearly supports a positive risk benefit profile of OAV101 which is expected to support registration covering a broad range of SMA patients. We remain committed to leading innovation in SMA treatment through our one-time gene therapies, uniquely designed to replace the function of the missing or defective *SMN1* gene."

"Maintaining motor function is a key goal for many older patients with SMA. This may allow them the capacity to continue to propel their electric wheelchair, feed themselves with intact hand to mouth function, and perform other activities of daily living as independently as possible" said Crystal Proud, M.D., Pediatric Neurologist and a Principal Investigator at Children's Hospital of the King's Daughters.OAV101 IT administration has not only been demonstrated to maintain motor function, but also increased it in indicating the impact a one-time therapy could have."

Results from STEER build on the Phase I/II open-label STRONG study which showed that treatment with OAV101 IT led to a clinically meaningful increase in HFMSE scores in one year,[7] and a clinically meaningful response in patients aged two to five years with SMA Type 2, who were able to sit but had never walked independently.[7] The results from the Phase III STEER study add to the clinical data and emerging real-world evidence for the use of one-time gene therapy to treat SMA.

STEER Study
STEER is a Phase III randomized, double-blind, sham-controlled study to evaluate the clinical efficacy, safety, and tolerability of a one-time dose of intrathecal onasemnogene abeparvovec (OAV101 IT) in treatment naïve patients with SMA Type 2, aged two to less than 18 years who were able to sit, but had never walked independently.[1] The therapeutic effect of OAV101 IT was evaluated using the Hammersmith Functional Motor Scale - Expanded (HFMSE) scores.[1] This is a validated assessment tool specifically designed to evaluate motor abilities and disease progression in patients with SMA. Secondary objectives included evaluating safety and efficacy of OAV101 IT using the Revised Upper Limb Module (RULM) scale.[1] More than 100 patients were randomized to receive OAV101 by IT injection or to receive a sham procedure.[1] At the end of the 52-week period, all eligible patients who received the sham procedure received OAV101 IT and all eligible patients who received OAV101 IT received the sham procedure.[1]

About OAV101 IT
Intrathecal onasemnogene abeparvovec (OAV101 IT) is an investigational, one-time gene therapy for patients with spinal muscular atrophy (SMA). OAV101 IT was evaluated in three clinical studies, including the Phase III STEER study, Phase I/II STRONG study and the Phase IIIb STRENGTH study.[1,7,8,9] The STEER study was a randomized, double-blind, sham-controlled study to evaluate the clinical efficacy, safety, and tolerability of OAV101 IT in treatment naïve patients with SMA Type 2, aged two to less than 18 years who were able to sit, but had never walked independently.[1] The STRENGTH study was an open-label, single arm, multi-center study evaluating the safety, tolerability and efficacy of OAV101 IT in patients with SMA who had discontinued treatment with nusinersen or risdiplam.[9] The STRONG study was an open-label, dose ranging study evaluating the safety and efficacy of OAV101 IT in patients with SMA with 3 copies of SMN2 aged 6 months to less than 60 months. The OAV101 IT clinical development program was studied in a broad population of approximately 170 patients with SMA and follow-up was conducted for up to 6.4 years.[10]

Novartis has an exclusive, worldwide license with Nationwide Children's Hospital to both the intravenous and intrathecal delivery of adeno-associated virus 9 (AAV9) gene therapy for the treatment of all types of SMA; 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.

About Spinal Muscular Atrophy
Spinal muscular atrophy (SMA) is a rare, genetic neuromuscular disease caused by a lack of a functional SMN1 gene, resulting in the irreversible loss of motor neurons, affecting muscle functions, including breathing, swallowing and basic movement.[11-14] The severity of SMA varies across a spectrum of types that each correspond to the copy number of the SMN2 gene, which produces a small fraction (~10%) of functional SMN protein compared with SMN1.[12] Loss of motor neurons cannot be reversed, so patients with SMA with symptoms at the time of treatment will likely require some supportive respiratory, nutritional and/or musculoskeletal care to maximize functional abilities.[13]

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,” “committed,” “investigational,” “remain,” “ongoing,” or similar terms, or by express or implied discussions regarding intrathecal onasemnogene abeparvovec (OAV101 IT), or regarding potential future revenues from OAV101 IT. 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 OAV101 IT 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 OAV101 IT will be commercially successful in the future. In particular, our expectations regarding OAV101 IT 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; 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’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 an innovative medicines company. Every day, we work to reimagine medicine to improve and extend people’s lives so that patients, healthcare professionals and societies are empowered in the face of serious disease. Our medicines reach more than 250 million people worldwide.

Reimagine medicine with us: Visit us at **https://www.novartis.com** and connect with us on **LinkedIn**, **Facebook**, **X/Twitter** and **Instagram**.

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