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PRESS RELEASE

New Novartis Phase III data demonstrate meaningful efficacy and safety results of intrathecal onasemnogene abeparvovec in broad patient population with SMA

- *Treatment with investigational OAV101 IT led to statistically significant 2.39-point improvement on the HFMSE vs. 0.51 points in sham control arm*
- *Safety findings were consistent in both treatment-naïve and treatment-experienced patients*
- *These new data indicate the potential for OAV101 IT to be a clinically meaningful treatment option for a broad range of patients with SMA*
- *Novartis plans to file applications with regulatory agencies in H1 2025*

Basel, March 19, 2025 – Novartis announced positive safety and efficacy results from the Phase III program for investigational intrathecal onasemnogene abeparvovec (OAV101 IT) in a broad population of patients aged two to <18 years with spinal muscular atrophy (SMA). In the Phase III STEER study, treatment with OAV101 IT led to a statistically significant 2.39-point improvement on the Hammersmith Functional Motor Scale Expanded (HFMSE), a gold standard for SMA-specific assessment of motor ability and disease progression, vs. 0.51 points in the sham control arm (P=0.0074).[1-5] In the Phase IIIb STRENGTH study, treatment with OAV101 IT in patients who have discontinued treatment with nusinersen or risdiplam demonstrated stabilization of motor function over 52 weeks of follow-up.

These data will be presented during the Muscular Dystrophy Association (MDA) Clinical and Scientific Conference held in Dallas, Texas, from March 16–19, 2025. The results add to the growing body of evidence within the OAV101 IT development program, which has evaluated a broad population of over 170 patients with SMA, spanning a total of over 6.4 years across the STEER, STRENGTH and Phase I/II STRONG studies.[6]

“In the STEER study evaluating treatment-naïve patients, OAV101 IT demonstrated a statistically significant improvement in motor function across a broad SMA population,” said Crystal Proud, M.D., Pediatric Neurologist and a Principal Investigator at Children's Hospital of the King's Daughters. “These results – paired with those in the STRENGTH study – support the potential for OAV101 IT to be a meaningful treatment option for people living with SMA with a goal of maintaining or improving motor function through a one-time therapy.”

OAV101 IT is an investigational gene replacement therapy designed to directly address the genetic root cause of the disease by replacing the nonworking *SMN1* gene with a single dose.

It is the first investigational gene replacement therapy to provide clinical benefit in both children and young adults with SMA with a favorable safety profile, underscoring the potential of this therapy to provide patients the opportunity to avoid repeated treatment administration.

“The data presented today from our OAV101 IT program reinforce our belief in this therapy, which has the potential to have a meaningful impact on a broad range of people with SMA through its continuous benefit via a one-time dose,” said Shreeram Aradhye, M.D., President, Development and Chief Medical Officer, Novartis. “Together with patients, caregivers and healthcare professionals, we are committed to continuing to advance our mission to lead innovation in SMA treatment and broaden therapy options with our gene replacement therapies.”

STEER Study
In the registrational STEER study, efficacy and safety were studied 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. 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. One hundred twenty-six (126) patients received either OAV101 IT (n=75) or a sham procedure (n=51). Mean (range) age at dosing was 5.89 (2.1–16.6) years in the treatment group and 5.87 (2.4–14.2) years in the sham arm. At the end of the 52-week period, all eligible patients had received both OAV101 IT and the sham procedure.
Key findings:

- The trial met its primary endpoint of change from baseline to 52 weeks in HFMSE score, with OAV101 IT demonstrating a statistically significant 2.39-point improvement on the HFMSE vs 0.51 points in the sham group (overall difference, 1.88 points; P=0.0074).
- All secondary endpoints consistently favor OAV101 IT, despite not achieving statistical significance due to the pre-planned multiple testing procedure.
- The overall incidence of adverse events (AEs), serious AEs (SAEs), and AEs of special interest was similar between both groups.

The most common AEs for both groups in the STEER study were upper respiratory tract infection and pyrexia. The most frequent SAEs were pneumonia and vomiting for the OAV101 IT group and pneumonia and lower respiratory tract infection for the sham group. Instances of transaminase increases were infrequent; most were low-grade and transient. There were no cases of Hy’s law.

STRENGTH Study
The open label Phase IIIb STRENGTH study evaluated the safety, tolerability and efficacy of OAV101 IT in patients with SMA aged two to less than 18 years who had discontinued treatment with nusinersen or risdiplam. In the study, 27 patients were enrolled with a mean (range) age of 7.4 years (2.4-17.7). Mean duration of prior risdiplam and nusinersen treatment were 2.98 and 4.32 years, respectively.
Key findings:

- OAV101 IT demonstrated a favorable safety profile that was consistent with STEER study.
- The motor endpoint of efficacy, HFMSE, demonstrated stabilization for the overall study population over 52 weeks.
    - The increase from baseline to 52 weeks in HFMSE least squares (LS) total score was 1.05.

All patients in the STRENGTH study experienced at least one AE. The most frequent AEs were common cold, pyrexia and vomiting. A total of 13 patients (48.1%) experienced AEs considered to be related to study treatment. No AEs leading to death or study discontinuation were reported.

About OAV101 IT
Intrathecal onasemnogene abeparvovec (OAV101 IT) is an investigational, one-time gene replacement therapy for patients with spinal muscular atrophy (SMA).

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 replacement 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 replacement 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.[11-13] The severity of SMA varies across a spectrum of types that generally correspond to the number of copies the individual has 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,” “would,” “expect,” “anticipate,” “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; 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 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 nearly 300 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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