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Novartis Community Update: Phase III STEER and Phase IIIb STRENGTH studies of OAV101 IT

Dear SMA Europe,

In response to your request, we are pleased to share an update on Novartis' Phase III STEER and Phase IIIb STRENGTH studies, evaluating investigational intrathecal onasemnogene abeparvovec (OAV101 IT) for the treatment of spinal muscular atrophy (SMA).

Topline results of STEER were announced in December 2024.[1] Results of STEER and STRENGTH were presented at the 2025 Muscular Dystrophy Association (MDA) Clinical and Scientific Conference in Dallas, Texas.

Data from STEER demonstrated positive safety and efficacy results for OAV101 IT in a broad population of patients aged two to <18 years with SMA.

STEER (NCT05089656) was a registrational study that assessed the efficacy and safety of investigational OAV101 IT in treatment naïve patients with SMA Type 2, aged two to <18 years who were able to sit, but had never walked independently.[2] Results showed:

- Treatment with investigational 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.[3-7]
- 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.

In the Phase IIIb STRENGTH study, treatment with OAV101 IT in patients who had discontinued treatment with nusinersen or risdiplam demonstrated stabilization of motor function over 52 weeks of follow-up.

STRENGTH (NCT05386680) was an open-label study evaluating the safety, tolerability and efficacy of OAV101 IT in patients aged two to <18 years with SMA who had discontinued treatment with nusinersen or risdiplam.[8] Results showed:

- 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 was 1.05 in HFMSE least squares (LS) total scores.

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.

For more information, please see our press release.

The STEER and STRENGTH 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.[9,10]

We plan to file applications with regulatory agencies in H1 2025 and are committed to working with stakeholders to make this therapy available to eligible patients as quickly as possible.

We thank you for your continued support and express our sincere gratitude to the patients, families and clinical investigators involved in the STEER and STRENGTH studies.

Kind regards,

Louise Strong
Patient Advocacy Novartis

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References:
1) Novartis. Available at: https://www.novartis.com/news/media-releases/novartis-intrathecal-onasemnogene-abeparvovec-phase-iii-study-meets-primary-endpoint-children-and-young-adults-sma. Accessed March 2025.
2) Clinicaltrials.Gov. Available at: https://clinicaltrials.gov/study/NCT05089656. Accessed March 2025.
3) Weber C, et al. *Brain and Dev*. 2024;46(5):89-198.
4) Coratti G, et al. *Eur J Neurol*. 2024;31:e16309.
5) Revised Hammersmith Scale for spinal muscular atrophy: A SMA specific clinical outcome assessment tool - PMC.
6) O'Hagen JM, et al. *Neuromuscul Disord*. 2007;17(9-10):693-697.
7) Mazzone E, et al. *Neuromuscul Disord*. 2014;24(4):347-352.
8) Clinicaltrials.Gov. Available at: https://clinicaltrials.gov/study/NCT05386680. Accessed March 2025.
9) Darras B. Intravenous and intrathecal onasemnogene abeparvovec gene therapy in symptomatic and presymptomatic spinal muscular atrophy: long-term follow-up study. Presented at the 29th International Annual Congress of the World Muscle Society, October 8–12, 2024, Prague, Czechia.
10) Clinicaltrials.Gov. Available at: https://clinicaltrials.gov/study/NCT03381729. Accessed March 2025.