Novartis International AG
Novartis Global Communications
CH-4002 Basel
Switzerland

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Community Statement from Novartis Gene Therapies: Clinical hold lifted paving way for Phase 3 trial to evaluate OAV-101 intrathecal (IT) in patients with spinal muscular atrophy (SMA)

Dear SMA Community,

Novartis Gene Therapies is committed to the SMA community and believes that all patients diagnosed with SMA should be able to benefit from the transformative impact of gene therapy. We are excited to announce that the U.S. Food and Drug Administration (FDA) has removed the partial clinical trial hold initiated in October 2019 and determined that our investigational compound OAV-101 IT clinical trial program for patients with SMA may proceed. Following this decision and input from the FDA and European Medicines Agency (EMA), Novartis now plans to initiate a new global Phase 3 registration-enabling study (STEER trial) to evaluate the clinical efficacy, safety, and tolerability of OAV-101 IT in treatment naïve patients with SMA who are between two and 18 years of age, able to sit, but have never walked. OAV-101 IT contains the same active ingredient as ZOLGENSMA® (onasemnogene abeparvovec-xioi), which is approved for intravenous use.

STEER is a randomized, double-blind, sham-controlled study. More than 100 patients will be randomized to receive OAV-101 by IT injection or to receive a sham procedure. At the end of the 52-week period, all eligible patients who received the sham procedure will receive OAV-101 IT, and all eligible patients who received OAV-101 IT will receive the sham procedure. This trial will add to the body of clinical data and emerging real-world evidence for the use of gene therapy to treat SMA. To find out more about the STEER trial, please contact the Novartis Gene Therapies Medical Information team at **medinfo.gtx@novartis.com**.

We will continue to invest in groundbreaking research and clinical trials to better serve the SMA community. We thank you for your continued engagement and will keep you updated on the latest information.

Please continue reading for Important Safety Information, and please see accompanying **Full Prescribing Information**, including Boxed Warning.

Sincerely,
Your Novartis Gene Therapies Team

About the STEER trial

- STEER is a Phase 3 randomized, double-blind, sham-controlled study to evaluate the clinical efficacy, safety, and tolerability of a one-time intrathecal (IT) dose of OAV-101 in treatment naïve patients with Type 2 SMA who are between two and 18 years of age, able to sit, but have never walked.
- The primary objective of STEER is to evaluate the efficacy of one-time IT administration of OAV-101 IT compared to sham control over a 52-week period, at the end of which patients in the control arm will be treated with OAV-101 IT. The therapeutic effect of OAV-101 IT will be evaluated using the Hammersmith Functional Motor Scale-Expanded (HFMSE).
- Secondary objectives include evaluation of safety and the efficacy of one-time IT administration of OAV-101 using the Revised Upper Limb Module (RULM) scale.

Questions & Answers

1. **Are you confident in OAV-101 IT as a potential treatment option for patients with SMA?**
   STEER will build upon promising data from the Phase 1/2 STRONG study, which to date has shown that treatment with OAV-101 IT led to significant increases in HFMSE scores and a clinically meaningful response. We believe that investigational OAV-101 IT is a viable potential treatment path for older patients with SMA and for whom a one-time, single-dose, treatment option could be especially compelling.

2. **Where will you be recruiting patients for this study?**
   Study plans for STEER are still being finalized. For more information about the study, contact the Novartis Gene Therapies Medical Information team at **medinfo.gtx@novartis.com**. It is important to clarify that enrollment is not anticipated to start until later this year.

3. **Why does the STEER trial use a sham control?**
   The use of a sham control offers an optimal chance of obtaining clear data that would allow for approval to treat more segments of the community.

4. **How did the results from the STRONG study inform the clinical trial design of STEER?**
   STEER will build upon the Phase 1/2 STRONG study, which showed that treatment with OAV-101 IT led to significant increases in HFMSE scores and a clinically meaningful response in older patients ≥2 years and <5 years old with SMA Type 2.

Indication and Important Safety Information for ZOLGENSMA® (onasemnogene abeparvovec-xioi)

What is ZOLGENSMA?
ZOLGENSMA is a prescription gene therapy used to treat children less than 2 years old with spinal muscular atrophy (SMA). ZOLGENSMA is given as a one-time infusion into a vein. ZOLGENSMA was not evaluated in patients with advanced SMA.

What is the most important information I should know about ZOLGENSMA?

- ZOLGENSMA can cause acute serious liver injury. Liver enzymes could become elevated and may reflect acute serious liver injury in children who receive ZOLGENSMA.
- Patients will receive an oral corticosteroid before and after infusion with ZOLGENSMA and will undergo regular blood tests to monitor liver function.
- Contact the patient's doctor immediately if the patient's skin and/or whites of the eyes appear yellowish, or if the patient misses a dose of the corticosteroid or vomits it up.

What should I watch for before and after infusion with ZOLGENSMA?

- Viral respiratory infections before or after ZOLGENSMA infusion can lead to more serious complications. Contact the patient's doctor immediately if you see signs of a possible viral respiratory infection such as coughing, wheezing, sneezing, runny nose, sore throat, or fever.
- Decreased platelet counts could occur following infusion with ZOLGENSMA. Seek immediate medical attention if the patient experiences unexpected bleeding or bruising.
- Thrombotic microangiopathy (TMA) has been reported to occur approximately one week after ZOLGENSMA infusion. Caregivers should seek immediate medical attention if the patient experiences any signs or symptoms of TMA, such as unexpected bruising or bleeding, seizures, or decreased urine output.

What do I need to know about vaccinations and ZOLGENSMA?

- Talk with the patient's doctor to decide if adjustments to the vaccination schedule are needed to accommodate treatment with a corticosteroid.
- Protection against respiratory syncytial virus (RSV) is recommended.

Do I need to take precautions with the patient's bodily waste?
Temporarily, small amounts of ZOLGENSMA may be found in the patient's stool. Use good hand hygiene when coming into direct contact with bodily waste for 1 month after infusion with ZOLGENSMA. Disposable diapers should be sealed in disposable trash bags and thrown out with regular trash.

What are the possible or likely side effects of ZOLGENSMA?
The most common side effects that occurred in patients treated with ZOLGENSMA were elevated liver enzymes and vomiting.

The safety information provided here is not comprehensive. Talk to the patient's doctor about any side effects that bother the patient or that don't go away.

You are encouraged to report suspected side effects by contacting the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch, or Novartis Gene Therapies, Inc. at 833-828-3947.

Please see the Full Prescribing Information.

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