SMA Community Update from Novartis Gene Therapies:
October 2021

Dear SMA Community:

Novartis Gene Therapies is committed to making a difference in the lives of people living with SMA and keeping the community informed of our progress along the way. In this update, we're sharing information about our key studies, publications and educational resources, and reflecting on recent events.

As always, thank you for your tireless dedication and partnership to advance care and treatment for patients with SMA. Together we are strong; together we are delivering.

With Gratitude,
YOUR NOVARTIS GENE THERAPIES TEAM

Connecting with the Community

This year, Novartis Gene Therapies was honored to sponsor and connect with many of you at the Annual CureSMA conference, EveryLife Foundation's Rare Disease Week on Capitol Hill and several CureSMA Walk-n-Rolls! We enjoyed seeing everyone who stopped by our booth and shared their stories. Thank you for your continued support of the rare disease community. We look forward to seeing you again at upcoming events.

Gene Therapy Education Resources

If you are interested in learning more about rare diseases and gene therapy, we encourage you to visit **exploregenetherapy.com** for information on how gene therapy works, educational resources from trusted organizations and so much more.

Recently Published Data

Lancet Neurology published data highlighting the **STR1VE-US** and **STR1VE-EU** studies.[1,2]

JAMA Neurology published findings from the **LT-001** study, which is an extension of the START trial.[3]

Access Snapshot for ZOLGENSMA® (onasemnogene abeparvovec-xioi) suspension, for intravenous infusion

98%[4]
OF US PATIENTS APPROVED FOR ACCESS

APPROVED IN OVER **40** COUNTRIES

OVER **1,400**[4]
PATIENTS TREATED GLOBALLY*

*Including clinical trials, commercially, and through the managed access programs

SMA Clinical Trial Program

ZOLGENSMA® Clinical Studies

START — Completed
Phase 1 study that evaluated safety and efficacy

STR1VE — Completed
Phase 3 study that evaluated safety and efficacy

SPR1NT — Ongoing
Phase 3 study evaluating safety and efficacy in presymptomatic patients

ZOLGENSMA® Long Term Follow-Up Studies

LT-001 — Ongoing
Monitoring ongoing safety of START study patients

LT-002 — Ongoing
Evaluating long term safety and efficacy of patients from clinical trials for SMA

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

SMA Clinical Trial Program

Investigational Studies

SMART

In April, Novartis Gene Therapies announced the SMART trial, a Phase 3b clinical study to further evaluate the safety, tolerability, and efficacy of intravenous ZOLGENSMA® in patients with SMA weighing ≥ 8.5 kg and ≤ 21 kg. The global study is expected to enroll 24 symptomatic children with SMA across sites in Europe, North America, Australia and Taiwan, and will follow patients for a period of 12 months. For more information please visit clinicaltrials.gov

STEER

In August, Novartis Gene Therapies announced the FDA lifted the partial clinical hold for our investigational intrathecal gene therapy clinical trial program. Novartis plans to initiate STEER, a global Phase 3, registration-enabling intrathecal clinical study in patients with SMA. The STEER trial will include treatment naïve patients between two and 18 years of age, able to sit, but have never walked.

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.

References

1. Day JW, et al. Onasemnogene abeparvovec gene therapy for symptomatic infantile-onset spinal muscular atrophy in patients with two copies of SMN2 (STR1VE): an open-label, single-arm, multicentre, phase 3 trial. *Lancet Neurol.* 2021;20(4):284-293.
2. Mercuri, E, et al. Onasemnogene abeparvovec gene therapy for symptomatic infantile-onset spinal muscular atrophy type 1 (STR1VE-EU): an open-label, single-arm, multicentre, phase 3 trial. *Lancet Neurol.* 2021;20(10):832-841.
3. Mendell JR, et al. Five-year extension results of the phase 1 START trial of onasemnogene abeparvovec in spinal muscular atrophy. *JAMA Neurol.* 2021;78(7):834-841.
4. Data on file. Novartis Gene Therapies, Inc. 2021.

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Bannockburn, IL 60015

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US-ZOL-21-0326