Genentech
A Member of the Roche Group

July 31, 2023

Dear SMA Community-

We are writing to share news following the Cure SMA Annual Conference that took place at the end of June. We enjoyed the chance to connect with so many of you over the course of the week and were thrilled to host an encore of the *DoubleTake* fashion show that was attended by more than 400 individuals. We are always so appreciative of opportunities to hear from the community on how we can improve our efforts and the conference this year was no exception!

The motivation behind the studies outlined below is driven by important questions raised by individuals living with SMA and their family members. Thank you for your partnership and engagement which truly inspires our ongoing progress.

Updates from The Cure SMA Research & Clinical Care Meeting June 28 – 30, 2023 included:

Investigating risdiplam treatment post gene-therapy

We have heard from the community that the approval of disease-modifying therapies in SMA has raised questions related to combination use and there is limited data currently available. In response, we have designed two new trials that will evaluate the use of risdiplam after gene therapy and shared overviews of those studies at both the Research & Clinical Care Meeting and Family Conference. New studies include:

- A Phase IV Open-Label Study Evaluating the Effectiveness and Safety of Risdiplam Administered as an Early Intervention in Pediatric Patients With Spinal Muscular Atrophy After Gene Therapy NCT05861986
- A Phase IV Open-Label Study Evaluating the Effectiveness and Safety of Risdiplam Administered in Paediatric Patients With Spinal Muscular Atrophy Who Experienced a Plateau or Decline in Function After Gene Therapy (NCT05861999)

Enrollment in the two Phase IV studies is expected to start in the second half of 2023, and clinical trial sites will be announced as soon as possible. For further information, including inclusion and exclusion criteria, please click on the ClinicalTrial.gov links provided above.

We hope these trials will provide important additional information on the safety and efficacy of risdiplam after gene therapy so that those living with SMA have the information they need to benefit from available therapies as much as possible.

Long-term efficacy and safety of risdiplam

New 4-year data from the ongoing FIREFISH study was also released at the conference and confirmed risdiplam's long-term efficacy and safety profile in children with Type 1 SMA. FIREFISH is a two-part study in babies aged 1-7 months at the time of enrollment. Additional information about the results can be found in our press release linked here.

Real-world evidence generation

- Results from a study assessing real-world outcomes among patients with SMA who have been treated with risdiplam were presented. Responses were captured via the 2022 Cure SMA Community Update Survey, a web-based questionnaire administered by Cure SMA annually,

and included findings across functional outcomes, health-related quality of life (HRQOL) and caregiver burden.[1]
- The design for a post-authorization effectiveness study (PAES) in patients with SMA treated with risdiplam in real-world settings was also presented.[2] The study will use secondary data from physician-reported SMA patient registries around the world and will compare outcomes for patients treated with risdiplam to those of patients not receiving any disease modifying therapy (DMT-naïve patients)
- Designs were presented for two non–interventional studies which aim to gather real-world evidence on the use of risdiplam in adults with SMA aged 25 and over, and in infants with SMA under two months of age. Study sites will be in the US.[3,4]

In conclusion

We hope that you find this update on what Genentech shared at the 2023 Conference helpful. Advances in our collective understanding of SMA treatment and care are thanks to all of your ongoing support and participation that help shape our forward thinking. Thank you for your continued partnership.The value of sharing insights, lessons and community connections cannot be overstated.

Sincerely,

Genentech SMA Team

What is Evrysdi?

Evrysdi is a prescription medicine used to treat spinal muscular atrophy (SMA) in children and adults.

Important Safety Information

- **Before taking Evrysdi, tell your healthcare provider about all of your medical conditions, including if you:**
    - are pregnant or plan to become pregnant, as Evrysdi may harm your unborn baby. Ask your healthcare provider for advice before taking this medicine
    - are a woman who can become pregnant:
        - Before you start your treatment with Evrysdi, your healthcare provider may test you for pregnancy
        - Talk to your healthcare provider about birth control methods that may be right for you. Use birth control while on treatment and for at least 1 month after stopping Evrysdi
        - **Pregnancy Registry.** There is a pregnancy registry for women who take EVRYSDI during pregnancy. The purpose of this registry is to collect information about the health of the pregnant woman and her baby. If you are pregnant or become pregnant while receiving EVRYSDI, tell your healthcare provider right away. Talk to your healthcare provider about registering with the EVRYSDI pregnancy Registry. Your healthcare provider can enroll you in this registry or you can enroll by calling 1-833-760-1098 or visiting https://www.evrysdipregnancyregistry.com.
    - are an adult male. Evrysdi may affect a man's ability to have children (fertility). Ask a healthcare provider for advice before taking this medicine
    - are breastfeeding or plan to breastfeed. It is not known if Evrysdi passes into breast milk and may harm your baby

[1] To TM , et al. A cross-sectional examination of outcomes data for risdiplam-treated individuals with SMA using the 2022 CURE SMA community update survey. Presented at Cure SMA Research & Clinical Care Meeting 2023
[2] Salem L, et al. A prospective, observational, long-term post-authorisation effectiveness study of risdiplam in patients with SMA. Presented at Cure SMA Research & Clinical Care Meeting 2023
[3] Shapouri S, et al. Real-world treatment with risdiplam in adults with SMA: a multicenter study. Presented at Cure SMA Research & Clinical Care Meeting 2023
[4] Moawad D, et al. Real-world use of risdiplam for the treatment of spinal muscular atrophy in infants under 2 months of age in the US. Presented at Cure SMA Research & Clinical Care Meeting 2023

- **Tell your healthcare provider about all the medicines you take**
- You should receive Evrysdi from the pharmacy as a liquid. If the medicine in the bottle is a powder, **do not use it**. Contact your pharmacist for a replacement
- Avoid getting Evrysdi on your skin or in your eyes. If Evrysdi gets on your skin, wash the area with soap and water. If Evrysdi gets in your eyes, rinse your eyes with water
- **The most common side effects of Evrysdi include:**
    - For later-onset SMA:
        - fever
        - diarrhea
        - rash
    - For infantile-onset SMA:
        - fever
        - diarrhea
        - rash
        - runny nose, sneezing and sore throat (upper respiratory infection)
        - lung infection (lower respiratory infection)
        - constipation
        - vomiting
        - cough

These are not all of the possible side effects of Evrysdi. For more information on the risk and benefits profile of Evrysdi, ask your healthcare provider or pharmacist.

You may report side effects to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Genentech at 1-888-835-2555.

Please see [accompanying] full Prescribing Information for additional Important Safety Information.

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