Genentech
A Member of the Roche Group

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Dear SMA Community-

We are writing in response to your standing request for updates related to Evrysdi® (risdiplam) and our clinical development program. As the season of gratitude is upon us we continue to be grateful for the many opportunities to connect with you and your families at local advocacy events and throughout the communities that we mutually live in and call home. As always, our work in SMA is evolving in direct response to the questions and suggestions that you raise to us so please do keep them coming!

First and foremost, we are thrilled to share the exciting news that Evrysdi® is now approved in over **100 countries** and more than **11,000 individuals globally living with SMA** have been treated with Evrysdi®, as of July 2023. It is with humility that we share this development, and in gratitude to the individuals who have taken part in our studies to date that led to our approval and our continuous understanding of SMA and risdiplam.

In other relevant news, we recently presented the primary analysis results from the RAINBOWFISH study which assesses the safety and efficacy of Evrysdi® in babies with pre-symptomatic SMA (n=26) aged from birth to 6 weeks.[1] The study included babies with 2 or more copies of the SMN2 gene. As you may recall, Evrysdi®'s approval was extended to include babies from birth to two months in May 2022 based on interim efficacy and safety data from the RAINBOWFISH study. Those results showed that the majority of pre-symptomatic babies treated with Evrysdi® achieved key milestones such as sitting and standing with half walking after 12 months of treatment.[2]

The results of the most recent data set are as follows:

- The study met its primary endpoint with 80% of the babies (n=5) able to sit without support for at least 5 seconds after 1 year of Evrysdi® treatment, assessed by the Bayley Scales of Infant and Toddler Development (BSID-III).
- The primary efficacy population included babies with 2 SMN2 copies and a CMAP amplitude of ≥1.5 mV at baseline. CMAP amplitude measures the muscle response to a stimulus, and a low score correlates with symptom onset in SMA patients and worse functional outcomes.
- Of the 26 babies in the study, 81% could sit independently for 30 seconds, including all patients with low CMAP amplitude at baseline (<1.5mV), and the majority were standing and walking.
- Adverse events (AEs) were more reflective of the age of the babies than underlying SMA. The majority of AEs were not considered treatment-related, and there were no deaths or AEs leading to withdrawal or treatment discontinuation. The most common AEs were teething, COVID-19, fever, inflamed digestive tract, eczema and constipation. The AEs observed in the RAINBOWFISH primary analysis are generally consistent with those AEs seen in other Evrysdi® trials in SMA.

Please be on the lookout for an end of year summary which will include a comprehensive list of developments from 2023. In the meantime, we hope you enjoy the holiday season with those for whom you are close. We again thank you for your ongoing support, guidance and partnership.

Sincerely,

Genentech SMA Team

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[1] https://www.gene.com/media/press-releases/15002/2023-10-03/majority-of-newborn-babies-with-spinal-m
[2] https://www.gene.com/media/press-releases/14955/2022-05-30/fda-approves-genentechs-evrysdi-risdipla

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
- **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.**