December 23, 2022

Genentech
A Member of the Roche Group

Dear SMA Community,

As the year comes to a close, we want to express our sincere gratitude for your ongoing collaboration, partnership and guidance. Your perspectives - whether as an individual living with SMA, family member or advocate - are absolutely vital in helping us understand and serve the needs of the SMA community.

In this spirit of gratitude, we have included a summary of 2022 developments completed in partnership with or service of the SMA community. Included in this overview are the advancements in research and clinical trials, product updates and broader initiatives.

Product Updates

- We are so pleased to share that in addition to serving the US SMA community, Evrysdi® (risdiplam) has now received regulatory approval in over 90 countries and has been used to treat **more than 8,000 patients worldwide**.
- This past May, the U.S. Food and Drug Administration (FDA) approved a label expansion for Evrysdi based on interim RAINBOWFISH study results to now include babies under two months old with SMA. This development means that Evrysdi is a prescription medicine used to treat SMA in children and adults. This includes SMA patients of all ages with Type 1, 2 or 3 SMA, including presymptomatic.
- In response to community concerns related to Evrysdi's storage requirements, we conducted a study which showed that, if necessary, Evrysdi can be kept at room temperature up to 104°F (up to 40°C) for a combined total of 5 days. This means that Evrysdi can be removed from and returned to a refrigerator, however, the total combined time out of refrigeration should not exceed 5 days. The updated information can be found in the latest U.S. Prescribing Information provided below.

Clinical Studies

*Completed Studies:*

- In February 2022, we were pleased to announce that the RAINBOWFISH study completed enrollment. Once the study participants have completed their 12-month trial period, researchers will analyze the overall study data, which we expect to receive in 2023. In March 2022, we announced positive interim results from RAINBOWFISH which supported the label expansion mentioned above for use in babies under two months of age.
- The following risdiplam studies have now completed enrolment: FIREFISH, SUNFISH, JEWELFISH and RAINBOWFISH.

*Investigational and Other Ongoing Studies:*

- Earlier this year, the first patient entered into Part 1 of the MANATEE clinical study – a two-part, global Phase 2/3 study evaluating the safety and efficacy of GYM329 (RO7204239), an investigational anti-myostatin antibody targeting muscular growth, in combination with risdiplam. Enrollment is currently ongoing across the eight sites that have opened, and our team continues to work to open recruitment at all remaining study sites. Results from Part 1 of the study will indicate if we move forward with Part 2 – the pivotal part of the study.

- We have initiated a new study to investigate the safety and effectiveness of a dispersible tablet formulation of risdiplam for the current oral liquid formulation (5mg) dose. If approved

by the FDA, the new formulation would be made available in addition to the current liquid formulation.

- We have also begun enrolling patients in the U.S. across 30 participating sites for the WeSMA study which aims to investigate the long-term safety and effectiveness of risdiplam. In this study, participants will be followed for up to 5 years from enrollment. Additional information about WeSMA and the other studies outlined above can be found at clinicaltrials.gov.

Scientific Presentations:
As part of our commitment to be transparent with the community and further our collective knowledge of SMA, we have regularly shared data from ongoing trials. Below is a summary of the data shared this year.

- **SUNFISH –** Three-year data on risdiplam's effectiveness in children and adults with Type 2 or 3 SMA was presented at the Muscular Dystrophy Association (MDA) Clinical and Scientific Conference in March. The long-term data from this study continues to support the original data in the USPI.
- **RAINBOWFISH –** Interim (preliminary) data exploring the use of risdiplam in pre-symptomatic babies was also presented at the MDA Clinical and Scientific Conference. The latest data supported the revision of the indication to include infants with SMA from birth to 2 months of age, formerly the indication was limited to patients 2 months of age and older. The indication extends to people that are symptomatic and presymptomatic.
- **FIREFISH** – Three-year data looking at risdiplam's effectiveness and safety in babies with Type 1 SMA was presented at the European Paediatric Neurology Society Congress in April. This data provided an updated primary efficacy analysis and also provided pooled efficacy analysis of parts 1 and 2.
- **JEWELFISH –** Two-year data evaluating risdiplam in children and adults with Type 1, 2 or 3 SMA who have previously been treated with other approved or investigational SMA-targeting therapies was presented at the World Muscle Society Congress in October. Results demonstrated that long-term safety was consistent with earlier studies.

Corporate Commitment Program
In furtherance of amplifying the voices of those living with SMA, earlier this year we partnered with 15 members of the SMA community and Open Style Lab. Together, we created "Double Take" — a prelude to New York Fashion Week aimed to increase disability visibility, break down stereotypes and champion adaptive fashion. The initiative reinforced the mission of *SMA My Way*.

The inclusive, anti-stereotype messaging behind Double Take helped advocate for meaningful change in the fashion industry, marking the importance of making fashion accessible to all. We were so pleased that Double Take was featured in **50+ national stories**, including *Vogue*. We are incredibly proud of this effort and grateful for the community's support in taking on this bold initiative.

We thank you for your continued commitment to partnering with us and wish you all a very happy holiday season and all the best for the New Year.

Sincerely,

Genentech SMA Team

(M-US-00018574)

## Indication

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. Talk to your healthcare provider right away if you become pregnant while taking Evrysdi. Ask about registering with the Evrysdi Pregnancy Registry, which was created to collect information about your health and your baby's health. Your healthcare provider can enroll you in this registry 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**.**