

MONTHLY Feature

FDA Approves New Treatment for SMA



On August 7, the US Food and Drug Administration (FDA) granted approval of risdiplam (Evrysdi) for the treatment of **spinal muscular atrophy (SMA)** in pediatric and adult patients. It is the third disease-modifying therapy approved to treat SMA, the leading genetic cause of infant death. Evrysdi is an SMN2-splicing modifier designed to help the SMN2 gene produce more functional SMN protein. The drug is an orally administered liquid, the first medicine that could be taken at home for individuals with SMA.

Clinical trials support approval

The FDA based its decision to grant approval to Evrysdi on the positive results of the pivotal FIREFISH and SUNFISH clinical trials.

The phase 2/3 FIREFISH trial was designed to assess Evrysdi's efficacy, safety, tolerability, pharmacokinetics, and pharmacodynamics in infants age 1 to 7 months with SMA type 1. The trial's first part (with a total of 21 participants) assessed the safety profile of Evrysdi and determined the dose for the second part. The second part (with a total of 41 participants) assessed efficacy as measured by the proportion of infants who could sit without support after 12 months of treatment, and longer, utilizing the Gross Motor Scale of the Bayley Scales

Read more about the approval of Evrysdi [here](#).

of Infant and Toddler Development-Third Edition (BSID-III). The study met its primary endpoint.

Results from the dose-finding first part of the phase 2/3 SUNFISH trial, which tested Evrysdi in a total of 180 patients age 2 to 25 years with SMA types 2 or 3, showed that treatment with Evrysdi led to a greater than two-fold increase in median levels of SMN protein in the blood after one year of treatment. The change from baseline in Motor Function Measure 32 (MFM-32) scale, the primary endpoint, was significantly greater in participants treated with Evrysdi compared to placebo. The strongest responses were observed in the youngest age group (2 to 5 years); 78.1% of participants who received

Evrysdi showed an increase of three or more points on the MFM-32 compared to 52.9% of participants who received placebo. However, results in older patients were not as positive; only 57.1% of participants age 18 to 25 years who were taking the drug experienced stabilization of their disease (compared to 37.5% on placebo). Statistically significant results were also seen in key secondary endpoints, including in the Revised Upper Limb Module (RULM), where a mean change from baseline was significantly greater in patients receiving Evrysdi compared with placebo.

There have been no treatment-related safety findings leading to study withdrawal in any Evrysdi trial. To date, more than 400 participants have been treated with Evrysdi.

Promising therapies

Approval of the therapy marks another milestone achievement for the SMA community. Now, in addition to Biogen's nusinersen (Spinraza) — the first disease-modifying therapy for SMA, which was approved in December 2016 — and Novartis AveXis' onasemnogene abeparvovec-xioi (Zolgensma) — a gene-replacement therapy for SMA that was approved in May 2019 — patients will have access to another promising therapy.