Daybue™ (trofinetide) – New orphan drug approval

- On March 10, 2023, Acadia Pharmaceuticals announced the FDA approval of Daybue (trofinetide), for the treatment of Rett syndrome in adults and pediatric patients 2 years of age and older.

- Rett syndrome is a rare, genetic neurological and developmental disorder. Patients with Rett syndrome experience a progressive loss of motor skills and language. Most babies with Rett syndrome seem to develop as expected for the first 6 months of life. These babies then lose skills they previously had attained at approximately 6 to 18 months of age – such as the ability to crawl, walk, communicate, or use their hands. Rett syndrome leads to severe impairments affecting nearly every aspect of life, including the ability to speak, walk, eat, and breathe.

    — Rett syndrome primarily affects females (1 in 10,000) and even more rarely affects males.
    — Acadia estimates Rett syndrome affects 6,000 to 9,000 patients in the U.S., with a diagnosed population of approximately 4,500 U.S. patients.

- Daybue is a synthetic version of a naturally occurring molecule known as the tripeptide glycine-proline-glutamate (GPE). The mechanism by which Daybue exerts therapeutic effects in patients with Rett syndrome is unknown.

- The efficacy of Daybue was established in a randomized, double-blind, placebo-controlled study in 187 patients with Rett syndrome 5 to 20 years of age. Patients were randomized to receive Daybue or matching placebo for 12 weeks. The co-primary efficacy measures were change from baseline after 12 weeks of treatment in the total score of the Rett Syndrome Behaviour Questionnaire (RSBQ) and the Clinical Global Impression-Improvement (CGI-I) score. RSBQ is a 45-item rating scale completed by the caregiver that assesses a range of symptoms of Rett syndrome (breathing, hand movements or stereotypies, repetitive behaviors, night-time behaviors, vocalizations, facial expressions, eye gaze, and mood). The CGI-I is rated by clinicians to assess whether a patient has improved or worsened on a 7-point scale.

    — The least-squares (LS) mean change from baseline to week 12 in the RSBQ score was -4.9 and -1.7 with Daybue and placebo, respectively (treatment difference -3.2, 95% CI: -5.7, -0.6; p = 0.018).
    — The mean week 12 CGI-I score was 3.5 and 3.8 with Daybue and placebo, respectively (treatment difference -0.3, 95% CI: -0.5, -0.1; p = 0.003).

- Warnings and precautions for Daybue include diarrhea and weight loss.

- The most common adverse reactions (≥ 10% of Daybue-treated patients and at least 2% greater than in placebo) with Daybue use were diarrhea and vomiting.

- Daybue should be administered orally twice daily, in the morning and evening, according to patient weight. Refer to the drug label for specific dosing recommendations.

- Acadia Pharmaceuticals plans to launch Daybue by the end of April 2023. Daybue will be available as a 200 mg/mL oral solution.