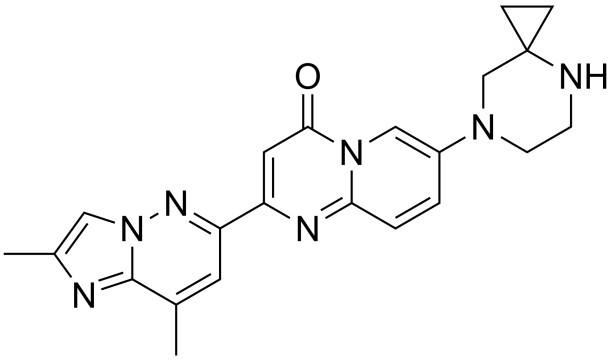
Brand Name: Evrysdi
Generic: risdiplam
Type: small molecule
Year Accepted/Phase: 2020

Mechanism:

Risdiplam is a small molecule that modifies the splicing of SMN2 pre-mRNA, leading to an increase in the production of functional SMN protein. This protein is essential for the survival and function of motor neurons, which are compromised in spinal muscular atrophy (SMA).

Chemical Structure:



Indication:

Evrysdi is indicated for the treatment of a broad spectrum of SMA types and patient ages.

Clinical trials:

FIREFISH Trial (Phase II/III)
Pubmed: https://pubmed.ncbi.nlm.nih.gov/33626251/
https://pubmed.ncbi.nlm.nih.gov/33626251/
Purpose: Evaluate the efficacy, safety, pharmacokinetics, and pharmacodynamics of risdiplam in infants with Type 1 SMA.
Dates: Part 1 results published in 2019; Part 2 results published in 2021.
Results:
Part 1 (Dose-finding): Determined the optimal dose for further studies.
Part 2 (Confirmatory): Demonstrated that risdiplam significantly improved motor function, with many infants achieving milestones such as sitting without support, and prolonged survival without permanent ventilation. This supported the FDA approval of Evrysdi for treating SMA in August 2020.

SUNFISH Trial (Phase II/III)
Pubmed: https://pubmed.ncbi.nlm.nih.gov/36735057/
https://pubmed.ncbi.nlm.nih.gov/34942136/
Purpose: Evaluate the efficacy, safety, and pharmacokinetics of risdiplam in children and young adults with Type 2 or Type 3 SMA.
Dates: Part 1 results published in 2019; Part 2 results published in 2020.
Results:
Part 1 (Dose-finding): Identified the appropriate dose for use in the confirmatory part of the trial.
Part 2 (Confirmatory): Demonstrated significant improvements in motor function compared to placebo, particularly in the Motor Function Measure 32 (MFM-32) scale, a measure of motor function in SMA patients. These results also contributed to the FDA approval of Evrysdi in August 2020.

JEWELFISH Trial (Phase II)
Pubmed: https://pubmed.ncbi.nlm.nih.gov/36780114/
Purpose: Evaluate the safety, tolerability, and pharmacokinetics of risdiplam in people with all types of SMA who previously received other SMA therapies.
Dates: Ongoing, with interim results published in 2020 and 2021.
Results: Interim data showed that risdiplam was well-tolerated and increased SMN protein levels across various SMA types, including in patients who had previously received other SMA treatments.

RAINBOWFISH Trial (Phase II)
Purpose: Investigate the efficacy, safety, pharmacokinetics, and pharmacodynamics of risdiplam in infants with genetically diagnosed SMA who are presymptomatic.
Dates: Ongoing, with interim results expected to guide future approvals and treatment strategies.

Results: Early data suggested that early treatment with risdiplam could prevent the onset of symptoms and support normal motor development in presymptomatic infants with SMA.