

# The Rise and Fall of Relyvrio: Lessons learned about how a promising drug for ALS failed

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## Abstract

The approval, release, and subsequent retraction of Relyvrio, produced by Amylyx Pharmaceuticals, highlights several critical issues within the neurodegenerative disease treatment research and development enterprise. A drug intended for Amyotrophic Lateral Sclerosis (ALS), Relyvrio, was initially granted approval by the FDA in 2022 after a small Phase II study. Earlier this year, in a Phase III study, the drug failed to meet its primary endpoints. Despite promising early results and high hopes amongst patients, advocacy groups, and clinicians, and despite \$380 million in sales last year, the Phase III study revealed Relyvrio's failure to improve function, communication, and independence in ALS patients. Amylyx has since pulled Relyvrio off the market, and is currently attempting to reposition the active ingredients in Relyvrio – sodium phenylbutyrate and taurursodiol – as a treatment for other, much rarer neurodegenerative diseases: Wolfram Syndrome and Progressive Supranuclear Palsy. This article explores the conditions under which such a massive failure for such a promising drug could unfold. We explore the nature and ramifications of federal regulatory leniency in drug approval along with the notion of repurposing drugs ineffective for a primary indication as potentially useful for other neurodegenerative diseases as a means of saving face and retaining profitability.

## Background/Purpose

### 1. Ingredients

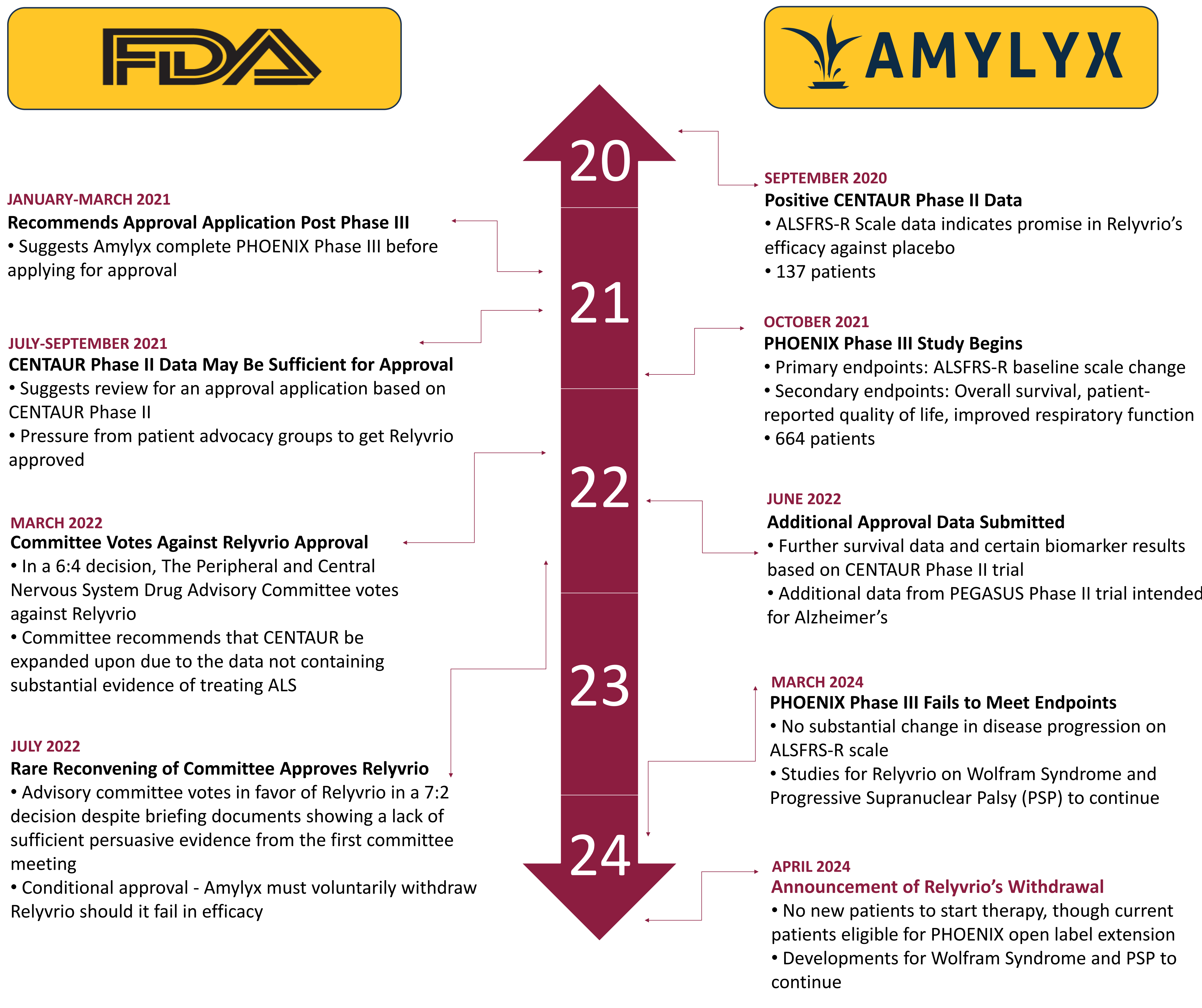
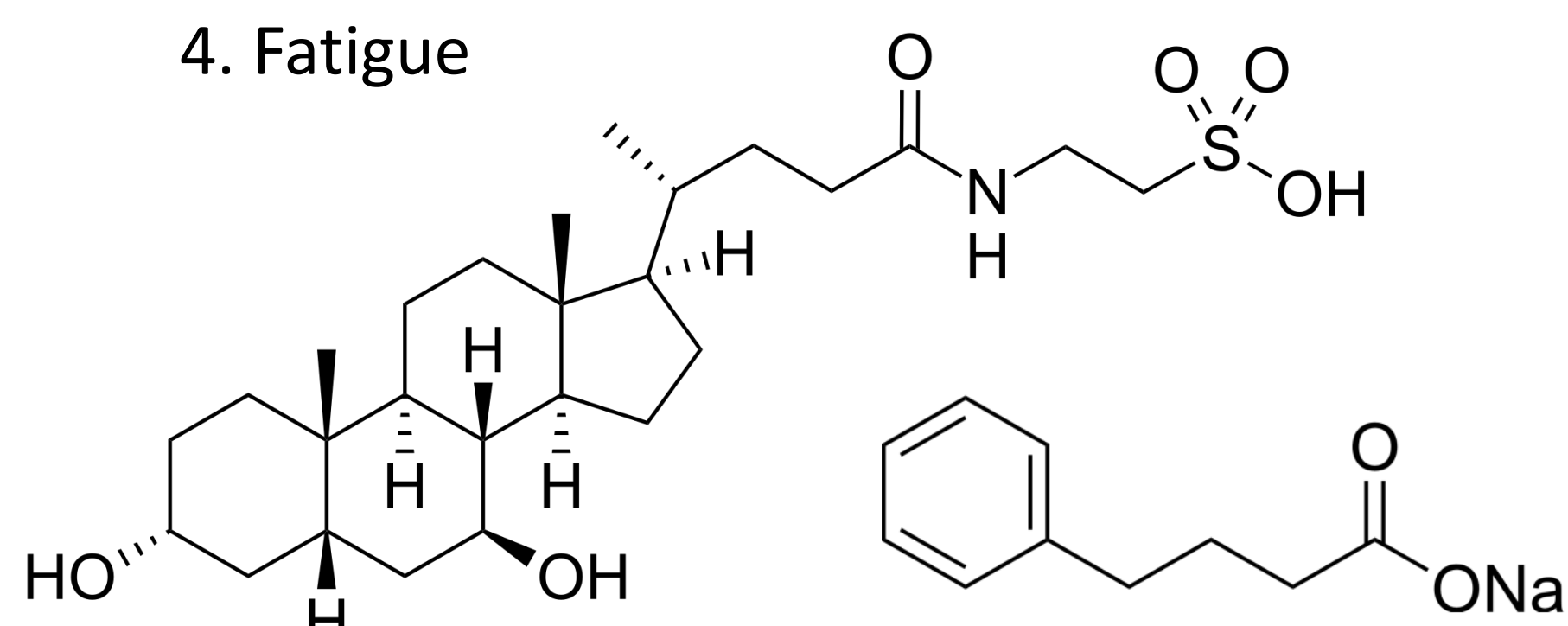
- Sodium Phenylbutyrate (PB)
- Tauroursodeoxycholic acid/Taurursodiol (TUDCA)

### 2. Intentions

- Treatment for Amyotrophic Lateral Sclerosis (ALS)
  1. ALS: a progressive neurodegenerative disease characterized by a rapid loss of muscle control, subsequent paralysis, and death. Involves the mass death of motor neurons.
  2. Pathogenesis similar to many neurodegenerative diseases (oxidative stress, mitochondrial and ER dysfunction, etc.)

### 3. Side Effects

- Minimal negative impacts
  1. Stomach and bowel pain
  2. Nausea
  3. Upper respiratory irritation
  4. Fatigue



## Discussion Questions

### Regulatory Approval and Process

1. What role does the reconvening or acceleration of approval play in balancing demand with the intense requirements of clinical trial?
2. Should regulatory bodies such as the FDA be more lax on approvals for drugs intended for diseases with high unmet needs?

### Ethics in Pharmaceuticals

1. What ethical and financial obligations do companies have when a drug shows initial promise but fails in final endpoints?
2. How do economic incentives influence the development and marketing especially for rare diseases like ALS, Wolfram Syndrome, or PSP?
3. Is using Relyvrio for Wolfram Syndrome and PSP a legitimate pathway to recover financial losses or make Relyvrio into a success?

### Societal Perspectives

1. How should advocacy groups navigate their support for experimental treatments in light of a failure such as Relyvrio?
2. How might the Relyvrio story impact public trust in the pharmaceutical industry? In the FDA?

### Policy and the Future of Neurodegenerative Disease Drug Research

What is driving the current model? Does it incentivize risk taking? Does it prioritize positive patient outcomes? How can it be improved so that we do not relive another Relyvrio?

## Key Ideas



- Relyvrio did not slow the progression of ALS or contribute to an overall better quality of life for patients

- Patient advocacy groups for diseases with high unmet treatment needs have an especially significant influence in the outcome of drug approval

- Amylyx is repurposing the active ingredients in Relyvrio for even rarer, more orphan diseases such as Wolfram Syndrome and Progressive Supranuclear Palsy (PSP)

## QR Code

