CRITICAL PATH INSTITUTE

Rare Disease COA Consortium Publication on Study Designs and Crafting Endpoints for Gene Therapy Development Programs in Rare Disease

C-Path's Rare Disease COA Consortium is delighted to share that "Study Designs and Crafting Endpoints for Gene Therapy Development Programs in Rare Disease: A Narrative Review" was published online in the November 2025 issue of *Advances in Therapy*.

Abstract

Gene therapies are emerging as a promising strategy for the treatment of rare genetic diseases, for which treatment options are often limited and do not address the underlying disease mechanisms. However, there are significant challenges for gene therapy programs, including defining a suitable first-in-human cohort and selecting endpoints with appropriate variability, sensitivity, reliability, and clinical meaningfulness; a systematic framework for the assessment and approval of these treatments is lacking. In this review, we share insights from 12 clinical development programs that culminated in recent approvals of gene therapies for rare genetic diseases (2016–2023). These approvals highlight useful strategies for navigating the unique challenges of gene therapy trials, including early and frequent engagement with regulatory bodies, incorporating the patient voice, selecting meaningful clinical outcome assessments and suitable controls, and leveraging well-matched real-world data to understand long-term efficacy, durability, and safety. By systematically documenting and analyzing detailed examples in this review, it becomes possible to derive data-driven solutions that can inform the design of future studies. Such solutions may diverge from prior assumptions or preconceptions but can provide a more evidence-based foundation for improving trial efficiency, and ultimately accelerate the development of urgently needed therapies for patients with rare genetic diseases.

Read the full publication here.