# Breaking Barriers for Rare Diseases

Center Forward Basics

March 2025

## Overview

With the Orphan Drug Act (ODA) entering its forty-second year in 2025, advocates and lawmakers are taking stock of the United States' progress in treating patients with rare diseases. Today, patients with rare diseases have shorter diagnostic journeys and more viable treatments than ever before. Despite this progress, hurdles continue as the gap between conditions and treatments remains significant, and some stakeholders believe the power of the ODA has decreased over time. Lawmakers and experts are searching for solutions to align what some say are misaligned incentives, improve the supply chain, and foster rare disease innovation which can provide hope to the 95% of rare disease patients without an FDA approved treatment while simultaneously ensuring those options are affordable when available.

In this Basic, we will give an overview of rare disease incentives, their impact, how they have changed over time, and what changes could be made in the future.

### Center Forward Basics

Center Forward brings together members of Congress, not-for profits, academic experts, trade associations, corporations and unions to find common ground. Our mission: to give centrist allies the information they need to craft common sense solutions.

For more information, please visit www.center-forward.org

## Rare Diseases and the ODA

Rare diseases are conditions affecting less than 200,000 Americans. While labeled “rare,” these conditions become quite prevalent in aggregate. Some estimates find somewhere between 7,000 to 10,000 identified “rare” diseases, affecting more than 30 million Americans. However, the comparatively small number of people suffering from each disease makes funding research for treatments less attractive for financial investment. In response to this problem, Congress passed the Orphan Drug Act (ODA) in 1983, providing financial incentives for rare disease treatments. In this respect, the United States is unique and has been at the cutting edge of rare disease science for decades. Initially, the legislation offered seven years of market exclusivity regardless of patent status, an exemption from FDA marketing application fees, and tax credits of up to 50% for research and development. Additionally, orphan drugs are not required to be sold at a discounted price to providers eligible for the 340B program, even for their non-orphan use. Finally, the FDA initiated 18 rare disease-specific programs to address some of the unique complexities of rare disease drug development. These provisions made research and development for rare diseases more financially viable, bringing new treatments to market.

## Underlying Challenges

Rare disease patients suffer complex diagnostic journeys. The lack of awareness of rare diseases, combined with a shortage of specialists and access barriers makes receiving a diagnosis for rare diseases a difficult process. The average time for an accurate diagnosis of a rare disease is 4.8 years but can reach up to 30 years in extreme cases. During this time, patients often see their conditions deteriorate with little knowledge about what is happening to them. Recent technological advances such as gene panels, microarrays, and exome sequencing have helped diagnose patients with rare diseases.

Research and development for pharmaceutical companies is a risky investment requiring immense startup capital. The percentage of drugs actually reaching the market is less than 2 percent, most of which fail during the “valley of death”. The Valley of Death describes the period when research is ongoing, but the drug is not commercially available. During this time,

pharmaceutical companies often require government financial support to sustain R&D efforts until the drug can turn a profit. A lesser known second valley of death often occurs when companies have difficulty collecting reimbursements after the drug is on the market.

The Priority Review Voucher (PRV) Program, a key incentive for rare disease drug development implemented in 2012, lapsed at the end of 2024. Originally introduced to encourage investment in treatments for neglected and rare pediatric diseases, the program granted pharmaceutical companies a voucher for an expedited FDA review of a separate drug. Under this program, sponsors receiving approval for a rare disease treatment also receive a voucher for a 6-month review of a drug instead of the FDA's standard 10-month review period. This transferable voucher system has historically provided significant financial value, sometimes selling for hundreds of millions of dollars to other drug manufacturers, making it an important driver for rare disease research. However, with its expiration, some industry stakeholders express concern the loss of this incentive could slow innovation and investment in orphan drug development.

## Results

Overwhelming evidence suggests the ODA has successfully facilitated the production of treatments for rare diseases and getting those treatments to patients. Before 1983, the Food and Drug Administration (FDA) approved 38 drugs to treat rare diseases. Since 1983, the FDA has granted over 1,100 approvals to treat rare diseases. The amount of orphan drug designations granted by the FDA has continued to increase over time. The last decade has seen nearly seven times as many designations as the first decade after the ODA's enactment. Developing rare disease treatments is an iterative process. The technology and science used to develop treatment for one disease often opens the door for finding novel treatments to other diseases in related areas. The ODA's structure allowing additional incentives for multiple designations, gives each dollar invested in rare disease research a compounding effect, helping develop treatments for both rare and common illnesses.

Pharmaceutical development resulting from the ODA has changed how doctors and patients think about some conditions, from untreatable to manageable. Cystic Fibrosis (CF) is a genetic disorder damaging the lungs, digestive system, and other organs. Patients with CF have mutations in their cells that produce mucus, causing blockages in the passageways and tubes of their bodies. In 1983, the life expectancy for patients with Cystic Fibrosis was ten years. From 2000 to 2021, the FDA granted 107 Orphan Drug Designations for treating CF. Today, the life expectancy is thirty-seven years. Sickle cell provides another success story. Sickle cell disease is a group of red blood cell disorders causing abnormal blood flow, leading to pain and other serious complications. Starting in 1979, the FDA began approaching various new treatments for sickle cell disease, raising the median age of survival from 28 to 43 years by 2017. Recently, in 2023, the FDA approved two gene therapies for sickle-cell, including the first CRISPR-based treatment, a technology research scientists use to selectively modify the DNA of living organisms to help make sickle cell disease more manageable for 100,000 American patients.

## Changes

While the Orphan Drug Act has helped bring many new treatments to the market, experts are concerned about the impact recent efforts to erode the ODA's incentives will have on rare disease drug research. In 2017, the Tax Cut and Jobs Act reduced the value of tax credits for rare disease research and development (R&D) from 50% to 25%. A majority of companies working in the rare disease space often spend most of their revenue, if not all of it, on R&D. Clinical research is inherently risky and expensive. More than 90% of experimental drugs do not result in an approved medicine. Rare disease research is even riskier. The substantial reduction in the orphan drug tax credit creates significant challenges, not just from an operational cash flow perspective, but ultimately in their financial viability as a business investing in rare disease research. Conversely, others may point to the fact some of the best-selling drugs in the world and highest expenditure Medicare drugs also have achieved at least one orphan designation, qualifying their manufacturers for ODA financial incentives.

Further complicating rare disease drug development is the Inflation Reduction Act of 2022 (IRA), which exempts orphan drugs with only one indication from the Drug Negotiation Program. The cap is intended to prevent drugs treating both rare and non-rare diseases from being exempt. However, some believe the current policy disincentivizes pharmaceutical

companies from pursuing additional rare disease indications of their orphan products for fear of losing their exemption.

## Proposals for Improvement

There are various policy proposals that could impact rare disease research. Some stakeholders argue for providing drug manufacturers with increased incentives. On rare disease day 2025, Representatives Josh Gottheimer (D-NJ) and Don Bacon (R-NE) reintroduced "Cameron's Law". The bipartisan legislation, named after Cameron Hyman, a ten-year-old boy diagnosed with Sanfilippo Syndrome, who has no approved treatment. This bill would restore the full value of the orphan drug tax credit to 50% for qualifying development expenses. Also in the 119th Congress, Representatives John Joyce (R-PA) and Don Davis (D-NC) introduced the ORPHAN Cures Act. This legislation seeks to alter the provision in the Inflation Reduction Act excluding rare-disease drugs with more than one approved indication from exempting the Drug Price Negotiations Program. The passing of this bill would allow rare-disease drugs with multiple rare indications to receive an exemption. Finally, Congressman Michael McCaul (R-TX) and a number of bipartisan cosponsors introduced the Give Kids a Chance Act, which would reauthorize the PRV program.

Other stakeholders have argued for alternate proposals such as tying overall drug revenues to tax incentives or extending 340B drug discounts to non-orphan indications in hopes for better financial alignment.

## The Path Forward

Today, new technologies are emerging for diagnostics, and more treatment options are available for rare disease patients than ever before. However, this progress could be challenged by a complex set of factors. Faced with these realities, policymakers will need to consider action to strengthen the United States' position at the forefront of rare disease innovation. Involving patient communities, medical experts, and industry will be key to producing a productive policy, which will ultimately lead to saving the lives of rare disease patients.

## Links to Other Resources

- Congress.gov: The Orphan Drug Act - Legal Overview and Policy Considerations
- Government Accountability Office: Rare Disease Drugs
- Health and Human Services Department: High-expenditure Medicare drugs often qualified for Orphan Drug Act incentives
- Johnson & Johnson - What is a Rare Disease
- NORD - Rare Disease Policy in Action
- NORD - The Orphan Drug Act Turns 40
- NORD - Understanding Rare Diseases
- National Library of Medicine - A Comprehensive Study of the Rare Diseases and Conditions Targeted by Orphan Drug Designations and Approvals Over the Forty Years of the Orphan Drug Act
- Summit Health - The Challenges of Treating Rare Diseases
- University of Chicago - The Orphan Drug Act at 35
- University of Southern California - Medicare's "Coverage with Evidence Development"