Rare Disease Company Coalition

#OneRareVoice

The Risks of Rare: Obstacles and Opportunities in Rare Disease Drug Development

A staggering 95 percent of rare diseases lack an FDA-approved treatment—and rare disease companies face unique risks in the race to discover, develop, and deliver treatments to patients. With high research and development (R&D) costs stretching into the millions and billions, and a long, challenging journey from development to market, rare disease companies rely heavily on private investment and product revenue to survive. Policy and regulatory decisions can strain an already-difficult investment thesis and threaten critical capital investments. These decisions ultimately make or break the ability for rare disease companies to deliver hope for the over 30 million Americans living with a rare disease.

RARE DISEASES IN THE U.S.

- **>10,000** Known rare diseases[1]
- **1 in 10** Americans live with a rare disease[2]
- **7.6 years** Average time to receive an official rare disease diagnosis[3]
- **$1 trillion** Cost on health care system annually[4]

Realities of Rare Disease Drug Development[5]

The journey from bench to bedside is even longer and more challenging for rare disease treatments than mass-market drugs.

- Smaller and diversified population sizes limit clinical trial initiation and progress, from recruitment to enrollment.
- A lack of understanding around disease progression has a significant impact on clinical outcomes.
- Regulatory inconsistencies can stall R&D at critical phases, disrupting or even ending development programs.
- It takes 3-5 years longer to bring an orphan drug to market than a mass-market drug.[6]

Rare disease companies are industry leaders in R&D investment.

- Both clinical- and commercial-stage rare disease companies invest over twice as much in R&D as their non-rare counterparts.
- Nearly 1 in 5 orphan drugs have historically been approved for additional orphan indications, only possible through time and additional R&D.
- While only a third of commercial-stage rare disease companies achieve profitability, these companies invest nearly a third of their annual revenue back into R&D.

Investors are listening—recent policy and regulatory changes have substantially reduced investments in rare disease companies.

- The trading index for rare disease companies has declined by nearly 7% per year over the last 5 years, compared to a 1.3% decline for non-rare disease companies.
- Rare disease companies saw nearly $10 billion less in investment available for research in 2022, stemming from decreases in venture capital investments, the IPO market, and partnership revenues.
- The decrease in private investment poses a serious threat to progress in rare disease drug development, as the private sector contributes $160 billion annually[7]—making up nearly 98% of total R&D funding.[8]

Policy at Play

In the decades since the passage of the Orphan Drug Act (ODA) in 1983, there has been significant progress in the number of approved orphan drugs—**from just 38 to more than 600 treatments for more than 1,000 rare diseases.**[9] Meaningful incentives have solidified private/industry investments in rare disease treatments, including expedited review pathways, user fee exemptions, tax credits, and extended exclusivity periods. These incentives have spurred the development of nearly 400 orphan drug indications in the last two decades. However, the progress made by these long-standing incentives is now at risk.

- **The Orphan Drug Tax Credit (ODTC)**, a cornerstone of the ODA, provides companies with a critical credit for qualified clinical testing costs. The tax credit, originally set at 50%, was halved in 2017; now, proposals seek to eliminate the credit once developers secure a second indication.
- **The FDA's Accelerated Approval Pathway (AAP)** is a regulatory pathway that recognizes the need for expedited evaluation of safety and efficacy for serious conditions with unmet need. The AAP is a vital resource for rare disease patients, but recent proposals to limit the pathway are threatening to impede patient access to potentially life-changing treatments.[10]
- **The Inflation Reduction Act of 2022 (IRA)** limits orphan drug exclusion from Medicare price negotiations to drugs with a single rare disease indication, discouraging investments as well as further R&D into existing approved drugs to address vastly unmet needs.
- **Prescription Drug Affordability Boards (PDABs)** establish systematic price controls that often undercut and devalue rare disease drugs. Eight states have implemented PDABs and many more are actively considering proposals.

Conclusion

Policymakers must recognize the unique risks, challenges, and costs associated with rare disease drug development. Blunt policies that weaken the case for investment in rare disease drug development will have a devastating and disproportionate impact on already underserved rare disease patients.

The RDCC strongly encourages policymakers to promote innovation and enable access to rare disease treatments by:

Co-sponsoring H.R. 5539, the ORPHAN Cures Act, H.R. 1350, Cameron's Law, and H.R. 1805, Leo's Law;

Ensuring consistent and appropriate use of regulatory flexibility across the FDA;

Bolstering the use of expedited approval pathways like accelerated approval; and

Reauthorizing the Pediatric Rare Disease Priority Review Voucher in 2024.

Methodology: *The Rare Disease Company Coalition (RDCC) commissioned a study,* 'Rare Disease Companies in the Public Markets: Challenging Performance Against a Backdrop of Policy Uncertainty,' *with Health Capital Group to examine the impact of policy challenges on investment in rare disease drug development. The study analyzed 700 publicly traded biopharmaceutical companies from mid-2018 to mid-2023.*

Use the QR code to access the full study and learn more.

[1] RAREX, The Power of Being Counted, 2022
[2] NIH, Genetic and Rare Disease Information Center
[3] Global Genes, Rare Disease Impact Report: Insights from patients and the medical community, 2013
[4] Every Life Foundation, The National Economic Burden of Rare Disease Study, 2021
[5] Health Capital Group Study, 2023
[6] CenterWatch, Tufts: Facing Many Challenges, Orphan Drugs Take 18% Longer to Develop
[7] The Brookings Institution, Who's Investing in Healthcare R&D?
[8] National Institutes of Health, Office of Budget
[9] NORD, New Study Investigates the Number of Available Orphan Products, Generics and Biosimilars, 2021
[10] NORD, FDA'S Accelerated Approval Pathway: A Rare Disease Perspective, 2021

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