Save Rare Treatments

Landscape Analysis: Investing in the Development of Rare Disease Treatments

Policy and market shifts in recent years have made it less attractive to invest in developing rare disease treatments.

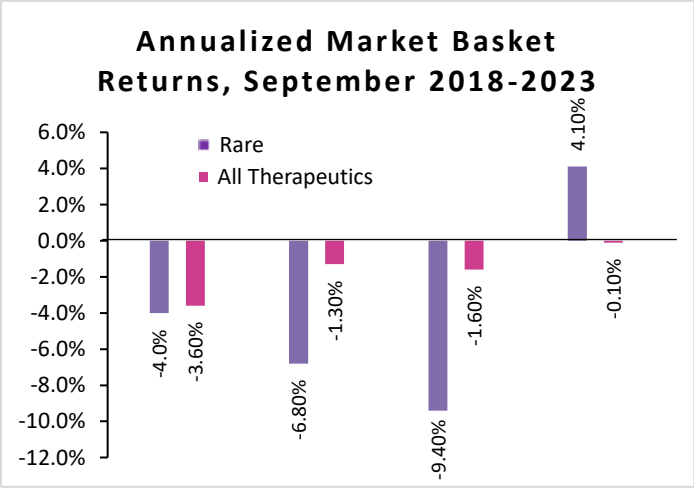
Policy Headwinds

Trends in policy development have created headwinds that diminish the likelihood of achieving favorable returns on investment in rare disease therapies, or orphan drugs. Several factors, taken together, have eroded investor confidence in the financial attractiveness of new investments in developing rare disease treatments:

- **The *Tax Cut and Jobs Act*, which substantially reduced existing tax credits for rare disease research and development (R&D)** from 50 percent to 25 percent. Furthermore, the Act stretched credit for these R&D expenses over five years, rather than the previous model of the full amount each year.
- **Increased policymaker and payer scrutiny of the FDA's Accelerated Approval program**, an important pathway for new rare disease drugs that allows for faster approval of drugs filling an unmet medical need.
- **The proliferation of state Prescription Drug Affordability Boards (PDABs)**, which may independently set upper payment limits (UPLs) and can restrict access to orphan drugs.
- **The implementation of the Orphan Drug Exclusion under the *Inflation Reduction Act*'s Medicare Drug Price Negotiation Program (MDPNP)**, which has created significant disincentives for the research and development of orphan drugs, especially for second and third indications.

Rare Disease Companies are Faring Worse with Investors, Compared to Non-Rare Companies

Traditional avenues for rare disease firms to access capital, such as the IPO market or acquisition by larger companies, are now less viable due to low interest rates and declining investor confidence.[i] In fact, the value of rare disease partnering deals plummeted by 25 percent in 2023, in contrast to the 9 percent rise in partnering activity for drug developers overall during the same period.[ii]



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Policy Changes are Compounding Existing Structural Challenges for Investment in New Rare Disease Treatments

Developing a rare disease treatment has always been challenging, but Policy changes like the MDPNP and market shifts have fostered a climate of hesitancy and risk aversion among potential investors considering investing in the rare disease sector. Factors that contribute to this hesitancy include:

- The average development time for a rare disease treatment exceeds 15 years, compared to ten years for non-rare treatments.[iii]
- Recruiting an adequate number of patients for clinical trials in diseases with very small patient populations can be lengthy and expensive.[iv]
- Revenues generated by rare disease therapeutics companies lag significantly behind those of non-rare firms, with less than one-third of commercial-stage rare disease companies with substantial revenues (more than $100 million annually) reporting profitability in 2022, compared to over half of their non-rare counterparts.[v]

Investment in treatments for rare diseases has degraded since the enactment of the Medicare Drug Price Negotiation Program's narrow Orphan Drug Exclusion.

Public Statements from Biopharmaceutical Manufacturers

Policy changes in the MDPNP are having a concrete impact on investment decisions. Several manufacturers have publicly cited the MDPNP's narrow Orphan Drug Exclusion as the reason they stopped work on drugs in development for the treatment of a rare disease.

- Alnylam announced it made the decision to pause a Phase III trial of its drug Amvuttra (vutrisiran) for a second indication of Stargardt Disease while it continued to evaluate the IRA's impact.[vi] [vii]
- Genentech said that, unless the MDPNP requirements change, it may have to delay application for a new drug for ovarian cancer for at least three years, so it can be approved simultaneously for both ovarian cancer and prostate cancer. This delay would allow the company the largest market for the greatest number of years.[viii]
- Relay Therapeutics announced in October 2023 the delayed development of a drug for a very rare form of cholangiocarcinoma until it could seek approval of the drug for a "larger, tumor-agnostic population."[ix]

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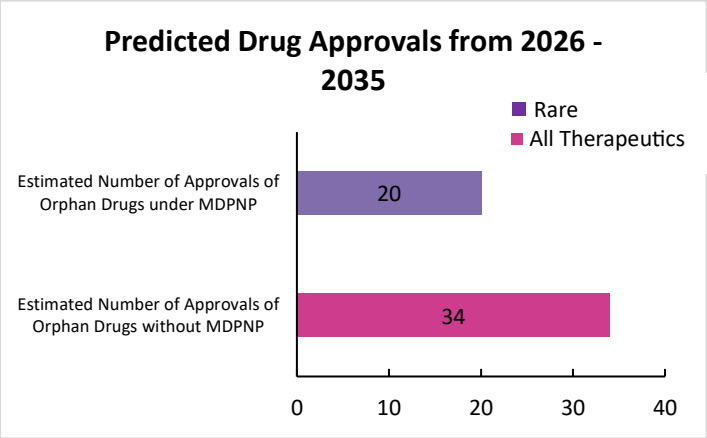
Challenges in Reporting

It is important to underscore the limited availability of *publicly* reported examples demonstrating the diversion of resources away from rare disease treatments. Many of these decisions are being made too early in the development pipeline to be *publicly* reported, so remain undisclosed.

Analyses Projects a Decline in the Number of Future Orphan Drug Approvals

A recent analysis of orphan drug approvals since 1983 shows that 15 percent of orphan drugs are approved for multiple rare diseases.[x] Yet, given the market and policy headwinds (including the Orphan Drug Exclusion in the MDPNP), analyses project a decline in FDA rare disease drug approvals. An orphan drug-specific analysis has predicted a 40 percent reduction in orphan FDA approvals from 2026 to 2035. Specifically, 14 of an estimated 34 orphan drugs from the manufacturing cohort analyzed will not come to market because of the new negotiation mechanism, and these reductions will primarily impact rare oncology treatments.[xi]



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[v] Id.

[vi] *Alnylam Pharmaceuticals Reports Third Quarter 2022 Financial Results and Highlights Recent Period Activity*. (2022, Oct 27). Alnylam. https://investors.alnylam.com/press-release?id=27046.

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