Novel Drug Approvals by the U.S. Food and Drug Administration in Rare Diseases: Findings from 2020–2023

Dubey A, Gupta P, Ray P, Kumar J, Shaikh J, Koumas A

INTRODUCTION

- Rare diseases, affecting fewer than 200,000 individuals in the United States, pose substantial challenges to healthcare systems worldwide. These conditions often lack effective treatment modalities, resulting in significant clinical and humanistic burden. [1]
- The emergence of novel therapies to address unmet needs holds the potential to revolutionize the landscape of rare diseases, ultimately improving patient outcomes and quality of life (QoL). [2]
- The U.S. Food and Drug Administration (FDA) Center for Drug Evaluation and Research (CDER) plays a crucial role in fostering innovations among pharmaceutical companies, evidenced by the rising number of novel drug approvals (NDAs) in recent years. [2]

OBJECTIVE

- This study aims to systematically review NDAs granted by the CDER for rare diseases between 2020 to 2023 and gain insights into rare disease drug development by analyzing the trends in these approvals.

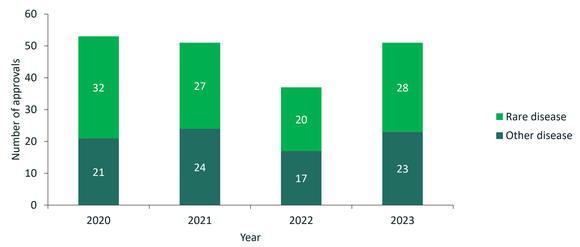
METHODS

- All novel drugs approved from 2020 to 2023 were identified using the FDA drug database.
- All NDAs were accessed on December 6, 2023, and reviewed to identify drugs indicated for rare diseases. Data was mainly collected from drug labels, approval letters, and FDA submission documents.
- A pre-specified data extraction template collated information regarding total number of NDAs, indication type, category of approval, regulatory pathways followed, and trial endpoints including patient-reported outcomes (PROs).

RESULTS

- A total of 192 novel drugs were approved by the FDA between 2020 and 2023; of which 55.7% of drugs pertained to rare diseases **(Figure 1)**.

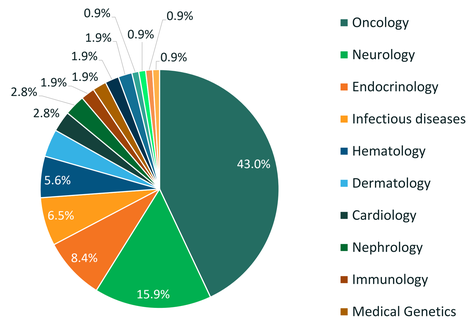
Figure 1. Number of novel drug approvals from 2020 – 2023



RESULTS (CONTINUED)

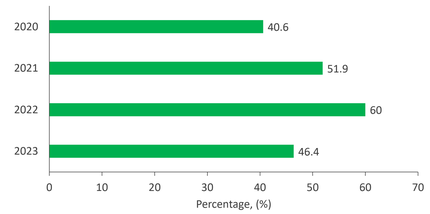
- Three foremost indications, including oncology (43.0%), neurology (15.9%), and endocrinology (8.4%), constituted approximately 67% of the total NDAs **(Figure 2)**.

Figure 2. Proportion of novel drug approvals by disease area



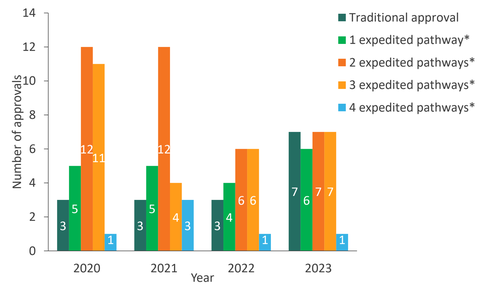
- Within oncology, 17.4% of the drugs were indicated for non-small cell lung cancer (NSCLC) and 15.2% drugs were indicated for multiple myeloma.
- Nearly half (48.6%) of NDAs comprised drugs categorized as first-in-class. The number of approvals for drugs with unique mechanisms of action has been increasing overall (40.6% in 2020, 51.9% in 2021, 60% in 2022, and 46.4% in 2023) **(Figure 3)**.

Figure 3. First-in-class approvals across years



- The FDA has developed four principal programs to expedite the drug development process: fast track, breakthrough therapy, priority review, and accelerated approval. These programs can be utilized individually or in combination.
  - From 2020 to 2023, 85.8% of the drugs were approved through one or more of the expedited development and review pathways **(Figure 4)**.

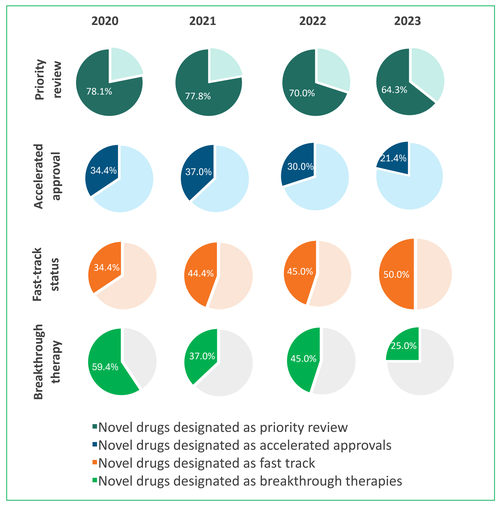
Figure 4. Utilization of expedited development and review pathways for novel drug approvals indicated for rare diseases



**Expedited pathways used singly or in conjunction: accelerated approval, fast track, breakthrough therapy, and priority review*

- Across all approvals from 2020 to 2023, 72.9% of drugs underwent priority review. However, the proportion of drugs assessed through this pathway decreased from 78% in 2020 to 64% in 2023 **(Figure 5)**.
- 41.1% of drugs had fast track designations, showcasing a notable rise from 34% in 2020 to 50% in 2023 **(Figure 5)**.
- Between 2020–2023, 33.3% received accelerated approval. However, during the same period, the proportion of drugs approved through accelerated pathways dropped from 34% to 21% **(Figure 5).**
- Breakthrough therapy designation was given to 41.1% of the drugs. The proportion of therapies reviewed through this pathway has decreased from 59.4% in 2020 to only 25% in 2023 **(Figure 5)**.

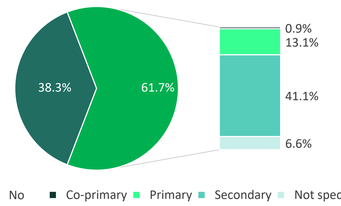
Figure 5. Proportion of approvals assessed through various regulatory pathways between 2020 – 2023



RESULTS (CONTINUED)

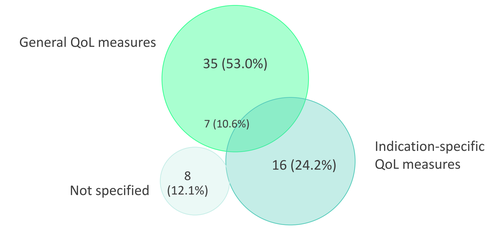
- Among 107 NDAs for rare diseases between 2020 and 2023, PROs were assessed in 61.7% (n=66) of the pivotal trials.
- The majority of trials assessed PROs as secondary or exploratory end points (41.1%, n=44), then primary endpoints (13.1%, n=14), co-primary endpoints (0.9%, n=1) and not specified (6.6%, n=8) **(Figure 6)**.

Figure 6. PROs assessment in rare disease trials of NDAs



- Across the 66 trials that conducted PROs assessments, 42 (63.6%) included generic QoL measures, and 23 (34.8%) included indication-specific measures **(Figure 7)**. EORTC-QLQ-C30, EQ-5D-5L, and FACIT scale were the most commonly used PRO assessment tools.

Figure 7. Utilization of various PRO measures in rare diseases across NDAs approved between 2020 – 2023



CONCLUSIONS

- This study demonstrates growing advancements and innovations in novel therapies for rare diseases, reflected by the increasing number of first-in-class therapies since 2020.
- The use of one or more of the expedited development and review pathways for novel drug approvals has been increasing overall. Specifically, fast-track review pathways have shown an upward trend.
- Insights generated from this study also revealed the crucial role of PROs, often as secondary endpoints, in assessing treatment efficacy and patients' well-being.

REFERENCES

1. US FDA. Rare Diseases at FDA. Accessed March 25, 2024. https://www.fda.gov/patients/rare-diseases-fda.
2. Miller KL, Fermaglich LJ, Maynard J. Using four decades of FDA orphan drug designations to describe trends in rare disease drug development: substantial growth seen in development of drugs for rare oncologic, neurologic, and pediatric-onset diseases. *Orphanet journal of rare diseases.* 2021;16(1):265. doi: 10.1186/s13023-021-01901-6

DISCLOSURES

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