Clinical Trial Evidence Supporting FDA Approval of Novel Agents (2022-2024)

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Introduction

Background: Clinical trial evidence at launch informs stakeholders and decision-makers on certainty, value, and coverage assessments. In 2025, the FDA announced that a single pivotal trial would become the standard, expecting to reduce development costs and accelerate time to market, with confirmatory evidence supporting marketing authorization.[1] Expedited FDA drug development and review programs further accelerates time to market, while potentially influencing the evidence available at launch.

Objectives: We evaluated and described pivotal clinical trials and regulatory approval characteristics of novel agents approved in Center for Drug Evaluation and Research (CDER) and Center for Biologics and Research (CBER) in 2022-2024.

Methods: Data on approved drugs were collected from FDA Drug Trial Snapshots, FDA labels, clinicaltrials.gov, and published manuscripts. We abstracted data on the number and Phase of pivotal clinical trials, number of participants enrolled, trial design, review type, and regulatory designations.

Approval Characteristics

2022

39 drugs approved*

- **59%** approved based on **1 pivotal trial** (mean: 1.6)
- Mean of **639 participants** (median: 153)
- **13%** (5/39) **gene/cell therapies**

2023

58 drugs approved*

- **67%** approved based on **1 pivotal trial** (mean: 1.4)
- Mean of **730 participants** (median: 206)
- **10%** (6/58) **gene/cell therapies**

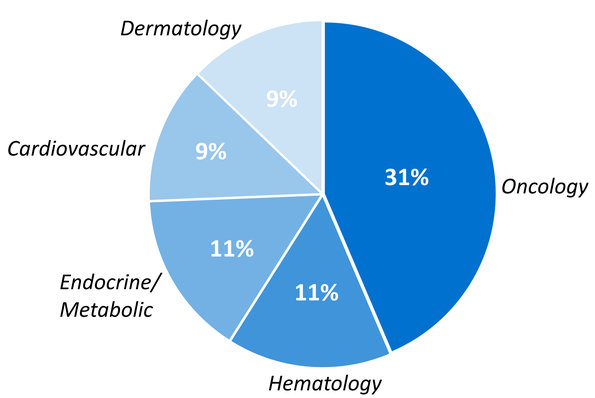
2024

54 drugs approved*

- **72%** approved based on **1 pivotal trial** (mean: 1.4)
- Mean of **559 participants** (median: 186)
- **11%** (6/54) **gene/cell therapies**

* From the list of novel agents, we excluded vaccines, antibiotics, microbiota products, blood or plasma-based products, and imaging or diagnostic agents.

Prevalent Therapeutic Areas of 2024 Approved Drugs†



† Areas not included (<5%): immunology, neurology, genitourinary, digestive, respiratory, mental/behavioral health, and infectious diseases.

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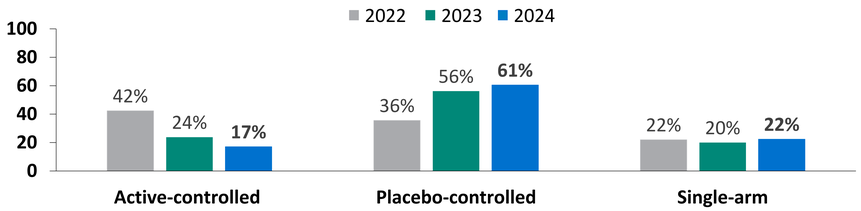
Clinical Trial Control Supporting Drug Approvals‡



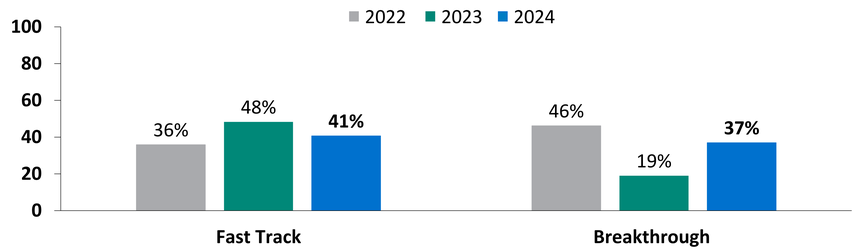
‡ We used a hierarchy structure to report the best trial control available for each drug (active-controlled, placebo-controlled, or single-arm).

Most drugs were approved based on randomized trial evidence, with over half supported by placebo-controlled trials in 2023 and 2024.

Notable decrease in the proportion of drugs approved based on active-controlled trials and corresponding increase in those approved based on placebo-controlled trials across the years.

Nearly one quarter of drugs were approved based on a single-arm trial.

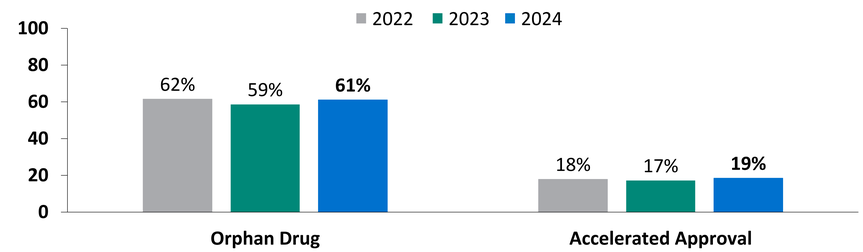
Fast Track and Breakthrough Designations



Fast track and breakthrough designations have varied across the years.

- **Fast track**: shortened review time for drugs treating serious conditions with unmet need (e.g., Exblifep® for UTIs).[2]
- **Breakthrough**: shortened review time for drugs demonstrating substantial improvements over current therapies for serious conditions (e.g., Nemluvio® for prurigo nodularis and atopic dermatitis).[2]

Orphan Drug Designations and Accelerated Approval



Orphan drug designations and accelerated approvals have been consistent across the years, and the majority of drugs received priority review (<50%).

- **Orphan drug:** drugs designed to treat rare diseases (e.g., Alhemo® for hemophilia).
- **Accelerated approval**: earlier approval of drugs for serious conditions based on surrogate endpoints (e.g., oncology drugs).[2]

Key Takeaways

Regulatory and approval characteristics of drug approvals were broadly consistent from 2022-2024. Key characteristics included:

- Frequent use of expedited drug designations and review pathways
- Most approvals were based on **one clinical trial**, with nearly a quarter supported by single-arm trials
- Frequent use of the accelerated approval pathway
- Significant **decrease in the proportion of drugs supported by active-controlled trials**

Key Implications

While trends highlight earlier FDA approval of innovative therapies, key implications include:

- **More uncertainty** of clinical trial evidence at launch
- Dependence on **more complex analyses** (e.g., indirect treatment comparisons) and assumptions
- **Shift comparative evidence generation** into post-approval period
- **Potential for variability** in payer decision-making or reimbursement

References

1. Prasad V, Makary MA. One pivotal trial, the new default option for FDA approval—ending the two-trial dogma. *N Engl J Med.* 2026;394(8):815–817. doi:10.1056/NEJMsb2517623.
2. Wright AC, McKenna A, Herce-Hagiwara B, Agboola F. Timing of health technology assessment in the United States: an evaluation of ICER reviews over eight years. *Institute for Clinical and Economic Review* (ICER).