Accelerating Rare disease Cures (ARC) Program

HOW CDER IS ACCELERATING RARE DISEASE CURES AND UPDATES ON THE PDUFA VII RARE DISEASE ENDPOINT ADVANCEMENT PILOT PROGRAM

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FDA U.S. FOOD & DRUG ADMINISTRATION

Disclosure

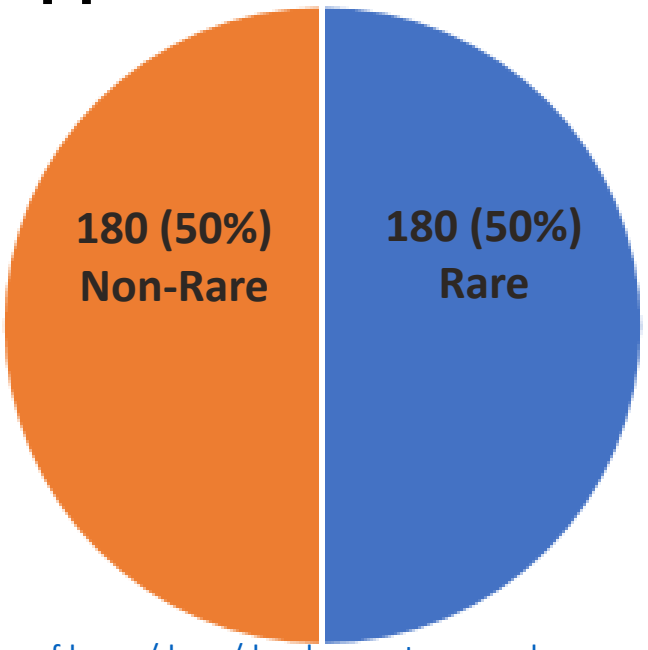
- This presentation is not intended to convey official US FDA policy, and no official support or endorsement by the US FDA is provided or should be inferred
- The materials presented are available in the public domain

Learning Objectives

- Discuss rare disease and orphan product approval trends
- Discuss challenges and considerations in rare disease drug development
- Share updates on CDER's Accelerating Rare disease Cures (ARC) Program and on CDER's Prescription Drug User Fee Act VII (PDUFA) rare disease commitment: Rare Disease Endpoint Advancement (RDEA) Pilot Program

Rare Disease Progress

Total CDER Novel Drug Approvals 2015-2022



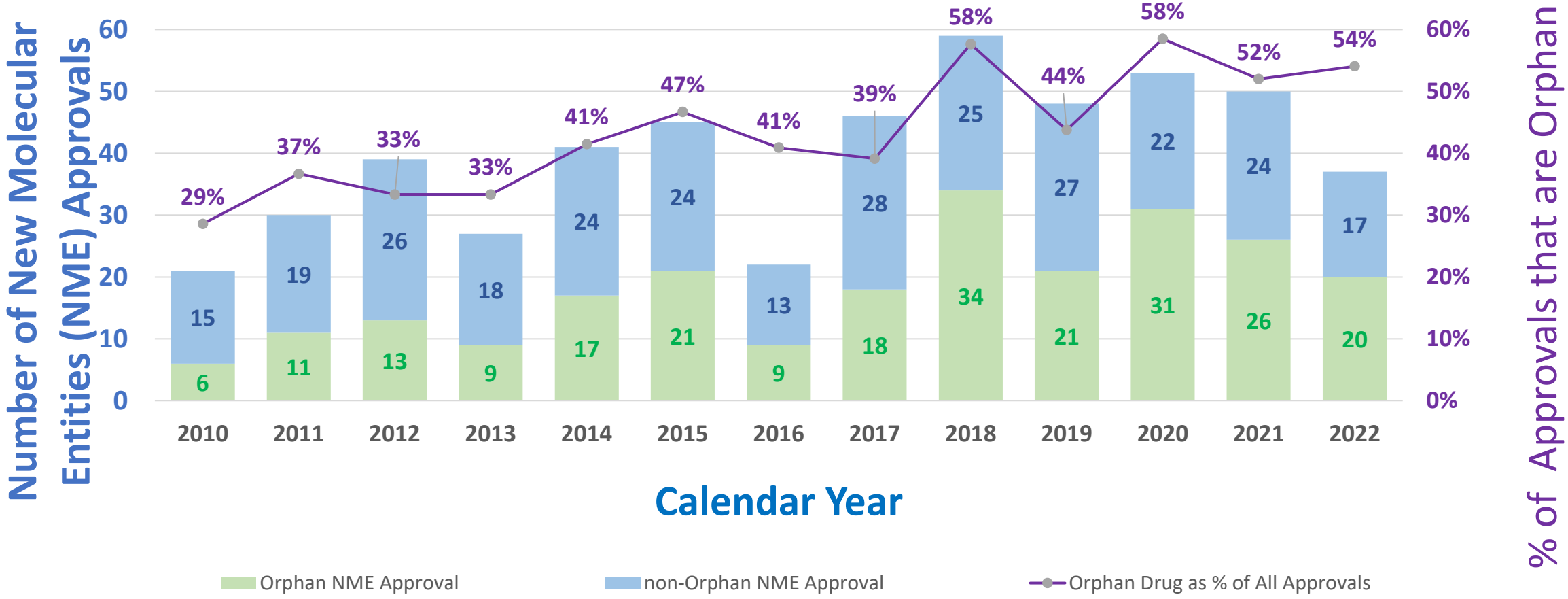
and… FDA has approved over 550 unique drugs and biologics for over 1,100 rare disease indications since the passage of the Orphan Drug Act (1983)

but… ~30 million Americans live with a rare disease

Vast majority do not have approved treatments

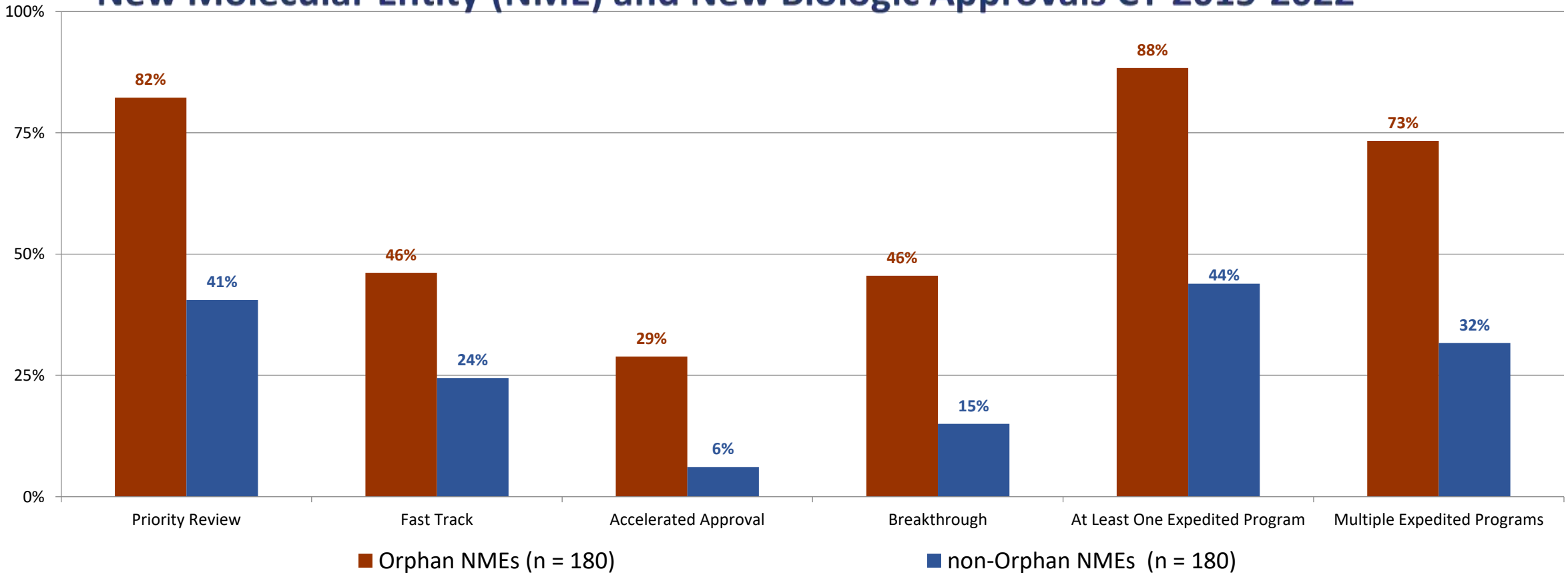
https://www.fda.gov/drugs/development-approval-process-drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products
https://www.fda.gov/drugs/news-events-human-drugs/cder-continues-advance-rare-disease-drug-development-new-efforts-including-accelerating-rare-disease
https://www.fda.gov/news-events/fda-voices/fda-continues-important-work-advance-medical-products-patients-rare-diseases#:~:text=The%20FDA%20will%20host%20its,medical%20products%20for%20rare%20diseases.

Proportion of CDER Novel Drug Approvals that are Orphan



CDER Use of Expedited Development Programs

New Molecular Entity (NME) and New Biologic Approvals CY 2015-2022



[Final Guidance: Expedited Programs for Serious Conditions – Drugs and Biologics 2014]

We Face Common Challenges in Rare Disease Drug Development

- **Natural history** is often poorly understood
- Diseases are progressive, **serious**, **life-limiting** *and* often lack adequate **approved therapies – urgent needs,** many have **pediatric onset**
- **Small populations** often restrict study design options
- **Phenotypic and genotypic** diversity within a disorder
- **Development programs often lack solid translational background**
- **Drug development tools** - **outcome measures** and **biomarkers** often **lacking**
- Lack of **precedent**, including **clinically meaningful endpoints**, for drug development in many rare diseases

And, Common Considerations in the "Environment" for Rare Disease Drug Development

- Many smaller companies with less regulatory experience
- Active patient stakeholder groups looking to navigate and participate in rare disease drug development
- A dedicated academic community that may have limited knowledge of regulatory requirements or aspects of clinical trial development

= We must engage our stakeholders to enhance their understanding, and gain their alignment and support

CDER'S Accelerating Rare disease Cures Program

- Vision

Speeding and increasing the development of effective and safe treatment options addressing the unmet needs of patients with rare diseases.

- Mission

CDER's Accelerating Rare disease Cures (ARC) Program drives scientific and regulatory innovation and engagement to accelerate the availability of treatments for patients with rare diseases.

CDER's Accelerating Rare disease Cures Program

CDER_ARC_Program@fda.hhs.gov

https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/cders-arc-program

ARC Year 1: Focus on Engagement

- FDA/NIH Regulatory Fitness in Rare Disease Clinical Trials conference, May 16-17, 2022
  - CDER's Rare Diseases Team and National Center for Advancing Translational Sciences (NIH)
  - Focus on academic investigators and those looking to learn how to bridge the gap between academic investigation and the regulatory aspects of drug development
- FDA and Duke Margolis Virtual Public Workshop: Translational Science in Drug Development: Surrogate Endpoints, Biomarkers, and More, May 24-25, 2022
  - CDER'S Office of Drug Evaluation and Science and Office of Clinical Pharmacology
  - Focus on translational science and the development of surrogate endpoints

ARC Year 1: Focus on Engagement

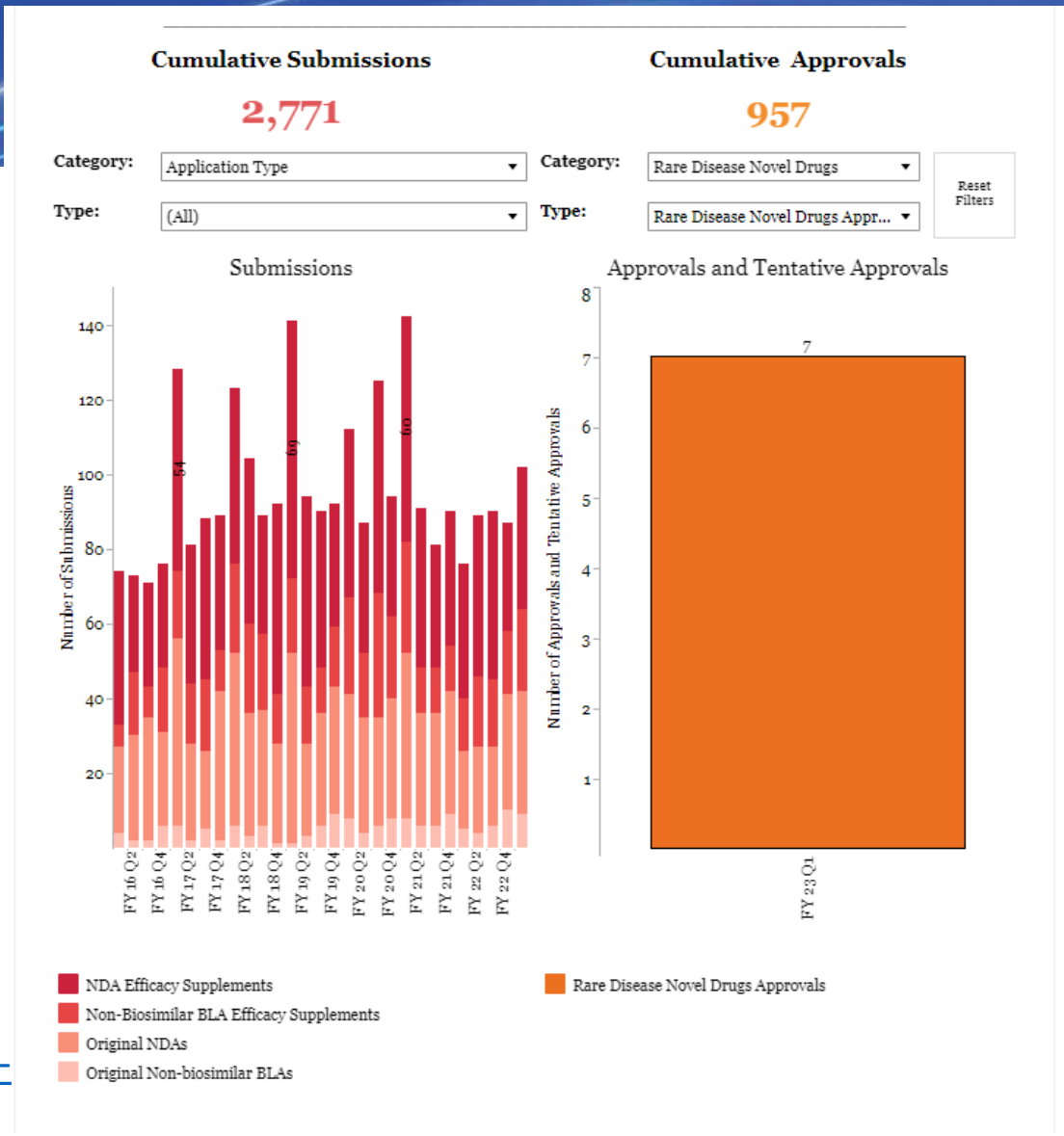
- FDA CDER & Johns Hopkins Center of Excellence in Regulatory Science and Innovation (CERSI) Workshop: Addressing Challenges in the Design and Analysis of Rare Disease Clinical Trials: Considerations and Tools, May 2-3, 2023
  - CDER's Rare Diseases Team and Office of Biostatistics
  - How to collect high quality and fit-for-purpose data for rare disease clinical trials
  - Use of real-world data to inform rare disease drug development
  - Design and analysis methodologies for use in rare disease clinical trials
- FDA CDER & University of Maryland Center of Excellence in Regulatory Science and Innovation (CERSI) Workshop: Creating a Roadmap to Quantitative Systems Pharmacology-Informed Rare Disease Drug Development, May 11, 2023

ARC YEAR 1: Patient Engagement for Rare Diseases

- CDER staff engaged in 23 Rare Disease Patient Listening Sessions
  - Held by Office of Commissioner's Patient Affairs Staff (PAS) or CDER's Professional Affairs and Stakeholder Engagement
  - https://www.fda.gov/patients/learn-about-fda-patient-engagement/fda-patient-engagement-opportunities
- CDER staff engaged in 19 Patient Focused Drug Development Meetings
  - https://www.fda.gov/drugs/development-approval-process-drugs/cder-patient-focused-drug-development
    - Email: PatientFocused@fda.hhs.gov

ARC YEAR 1: ARC's Quarterly Newsletter

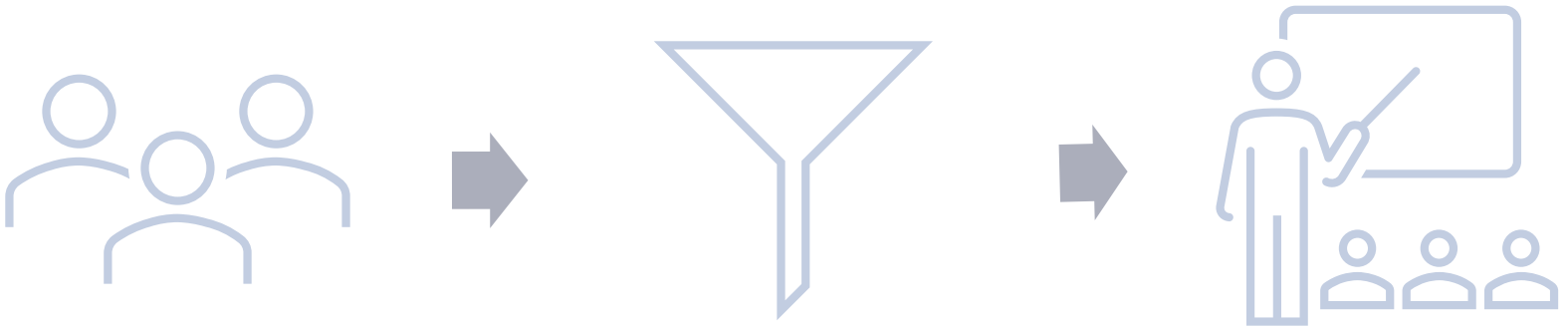
- To subscribe: U.S. Food and Drug Administration (govdelivery.com)



FDA-TRACK: Center for Drug Evaluation and Research: Drugs and Biologics https://www.fda.gov/about-fda/fda-track-agency-wide-program-performance/fda-track-center-drug-evaluation-research-pre-approval-safety-review-drugs-and-biologics-dashboard

LEARNING AND EDUCATION TO ADVANCE AND EMPOWER RARE DISEASE DRUG DEVELOPERS (LEADER 3D)

What is **LEADER 3D**?



CDER is seeking input from stakeholders who design or conduct rare disease drug development programs

Identify knowledge gaps for stakeholders about the regulatory process of rare disease drug development

Create or expand educational resources for stakeholders

LEADER 3D (CONT.)

- Better understand the challenges in bringing rare disease drug products to market.
- Identify knowledge gaps and produce educational materials on fundamental topics important to our stakeholders, such as:
  - Nonclinical and clinical pharmacology considerations
  - Clinical trial design and interpretation
  - Regulatory considerations for rare disease drug development
- In parallel with the LEADER 3D effort, CDER is working with the National Organization for Rare Disorders to develop an advanced drug development education series for patients and patient groups.

https://www.fda.gov/drugs/news-events-human-drugs/cder-continues-advance-rare-disease-drug-development-new-efforts-including-accelerating-rare-disease

Rare Disease Endpoint Advancement (RDEA) Pilot Program Overview

- Scope: The RDEA pilot program will seek to advance rare disease drug development programs by providing a mechanism for sponsors to collaborate with FDA throughout the efficacy endpoint development process. An endpoint, or endpoints, will be considered eligible for proposal submission to RDEA if each of the following criteria are met:
  - The associated development program **should be active and address a rare disease**, with an active IND or pre-IND for the rare disease
  - The proposed endpoint is a **novel efficacy endpoin**t intended to establish substantial evidence of effectiveness for a rare disease treatment

RDEA Pilot Program Overview (cont)

- **Submissions**: FDA will select a limited number of qualified proposals for admission into RDEA that increases after the first year of PDUFA VII:
  - *FY 2023*: Sponsors may submit proposals beginning in Q4, and FDA will accept a maximum of 1 proposal
  - *FY 2024 – FY2027*: FDA will accept up to 1 proposal per quarter with a maximum of 3 proposals per year
- **Transparency**:
  - FDA will conduct **up to 3 public workshops** by the end of FY 2027 to discuss various topics related to endpoint development for rare diseases
  - To promote innovation and evolving science, **novel endpoints developed through RDEA may be presented by FDA**, such as in guidance documents, on a public-facing website, or at public workshops, including prior to FDA's approval for the drug studied in the trail

RDEA Pilot Program Completion

- Sponsors who have completed the maximum of 4 RDEA meetings or do not have additional endpoint-focused questions or issues to discuss with FDA may proceed with the standard regulatory submission process.

- FDA's advice provided during and between RDEA meetings does not constitute a regulatory decision and is considered non-binding. Completing the 4 RDEA meetings does not guarantee approval for a regulatory submission that includes efficacy endpoints discussed during RDEA meetings.

- After completion of 4 RDEA meetings, the sponsor can request additional input from FDA, as needed, through other formal meeting mechanisms, such as Type B, Type C, Type C Surrogate Endpoint, or Type D meetings.

RDEA Updates

- Website: https://www.fda.gov/drugs/development-resources/rare-disease-endpoint-advancement-pilot-program
- FAQs
- Proposal Elements
- Meeting Package Elements
- Disclosure Elements
- Endpoint Development Resources

RDEA Virtual Public Workshop

- June 7 and 8, 2023; 1-5 pm - *VIRTUAL*
- Jointly hosted by FDA's Center for Drug Evaluation and Research, Center for Biologics Evaluation and Research, and the Duke-Margolis Center for Health Policy
- For more information and to register for this workshop, please visit https://healthpolicy.duke.edu/events/rare-disease-endpoint-advancement-pilot-program-workshop-novel-endpoints-rare-disease-drug
- Questions? Email RDEA.Meetings@fda.hhs.gov

Conclusions

- In recent years, over 50% of CDER's novel drug approvals were for rare diseases
- CDER's ARC program will help CDER work more effectively with our rare disease drug development partners
- CDER's ARC Program looks forward to sharing learnings from rare disease programs such as the PDUFA VII Rare Disease Endpoint Advancement Pilot Program

Challenge Question #1

- Looking at CDER novel drug approvals (2015-2022), approximately what percentage are for use in non-rare diseases vs what percentage in rare/orphan designated products?

A. 64% vs 30%
B. 50% vs 50%
C. 30% vs 64%
D. 44% vs 22%

Challenge Question #2

- The RDEA Program will provide the opportunity for sponsors to engage with the FDA on what aspect of drug development?

A. Model Informed Drug Development

B. Complex Innovative Design

C. Rare Disease Endpoint Advancement

D. All of the above