CDER's Perspective on Working Together with Our Rare Disease Partners within CDER and across FDA

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Disclosure

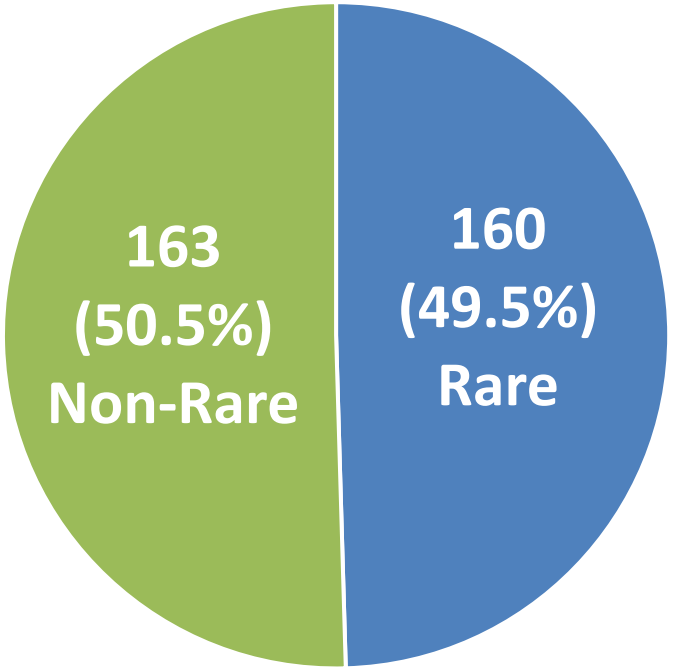
- This presentation is not intended to convey official US FDA policy, and no official support or endorsement by the US FDA is provided or should be inferred
- The materials presented are available in the public domain

Learning Objectives

- Discuss rare disease and orphan product approval trends and CDER's Organization
- Describe CDER's Rare Diseases Team and Prescription Drug User Fee Act VI (PDUFA) commitments
- Describe CDER's Prescription Drug User Fee Act VII (PDUFA) commitments: Rare Disease Endpoint Advancement (RDEA) Pilot Program
- Describe CDER's Accelerating Rare disease Cures (ARC) Program

Rare Disease Progress

Total CDER Novel Drug Approvals 2015-2021



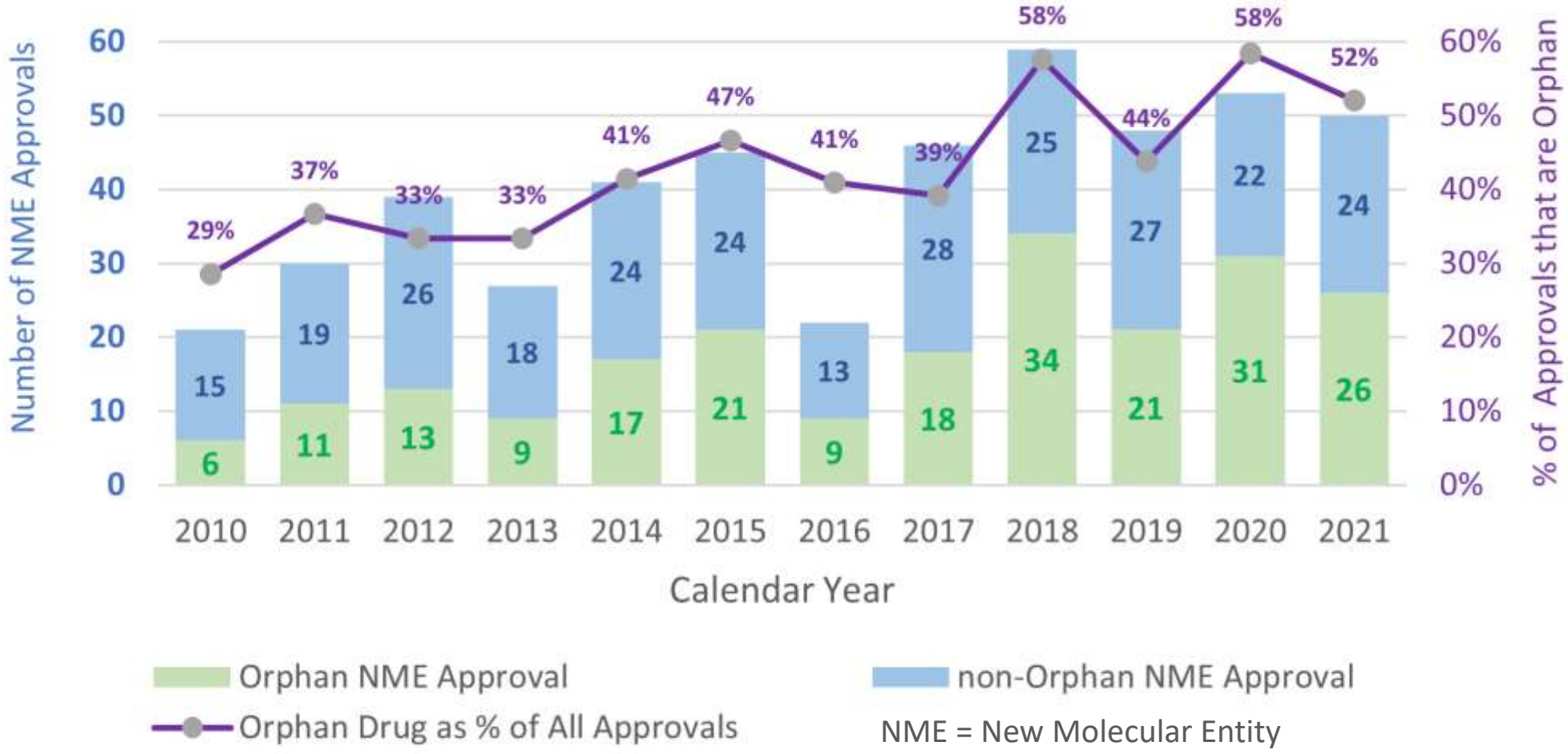
and… Over 600 treatments for rare diseases have been FDA-approved since the passage of the Orphan Drug Act (1983)

but… ~7,000 rare diseases

Vast majority do not have approved treatments

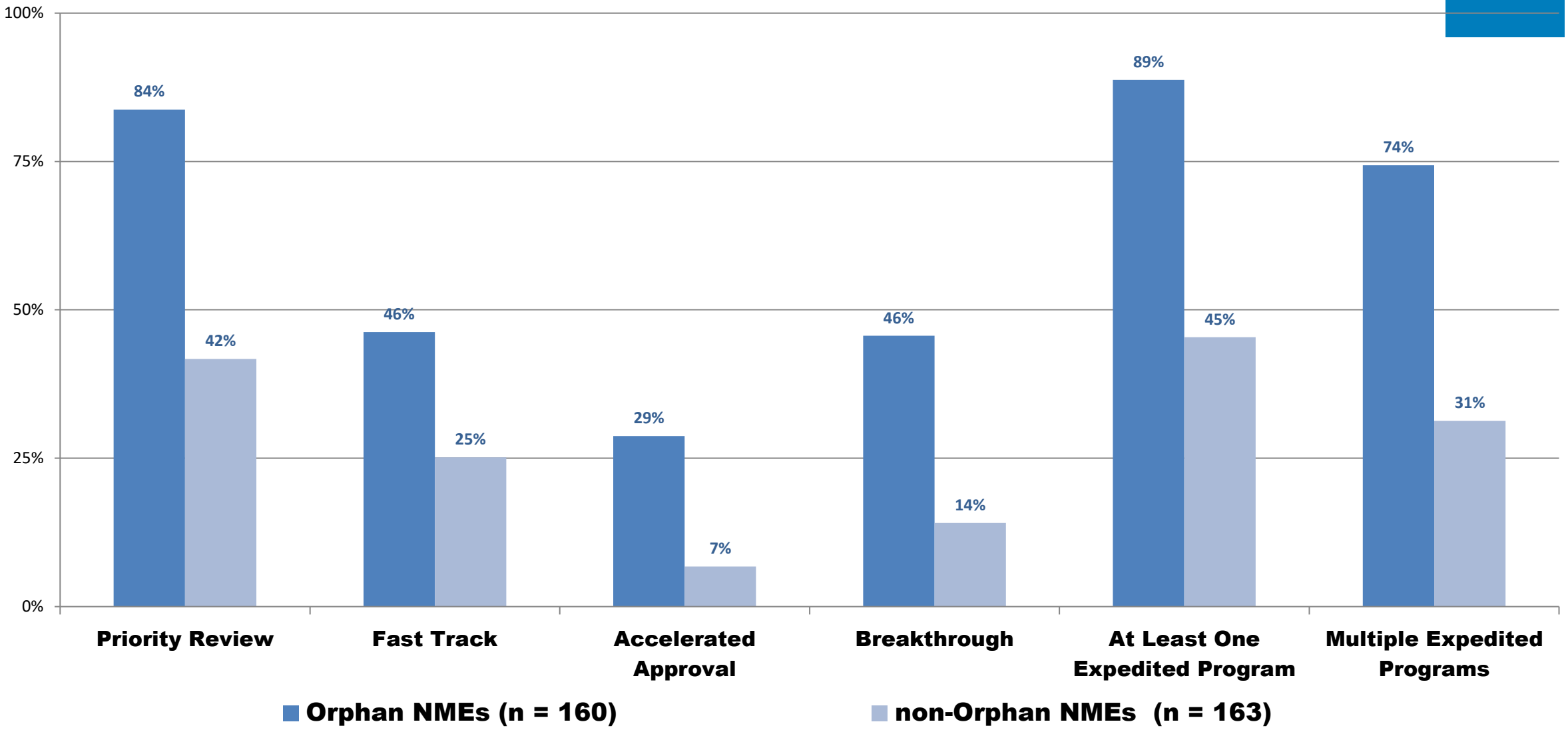
https://www.fda.gov/drugs/development-approval-process-drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products
https://www.fda.gov/industry/developing-products-rare-diseases-conditions

Proportion of CDER Novel Drug Approvals that are Orphan

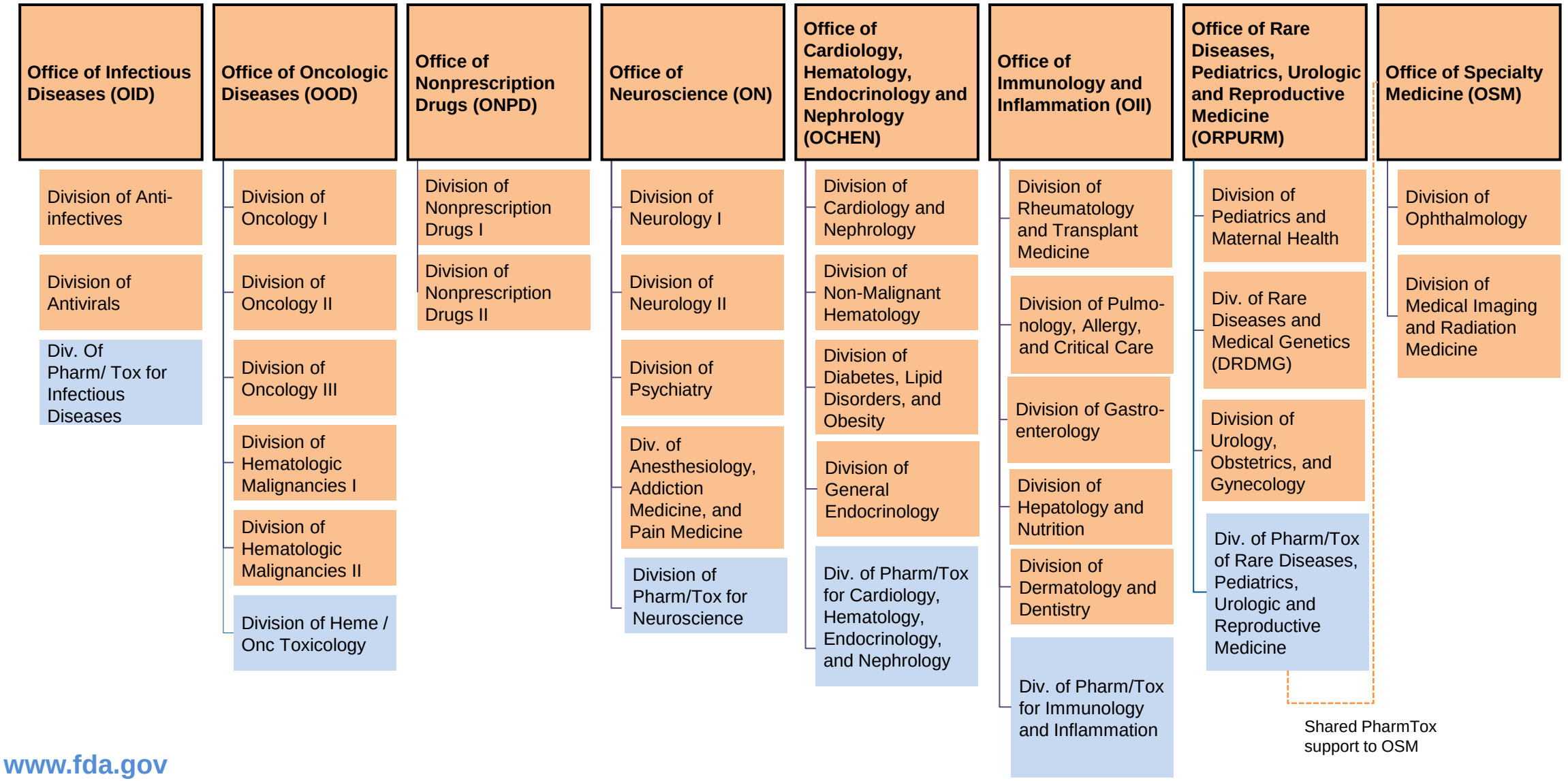


CDER Use of Expedited Development Programs

New Molecular Entity (NME) and New Biologic Approvals CY 2015 - 2021



Reorganization of CDER's Office of New Drugs (Clinical Offices)



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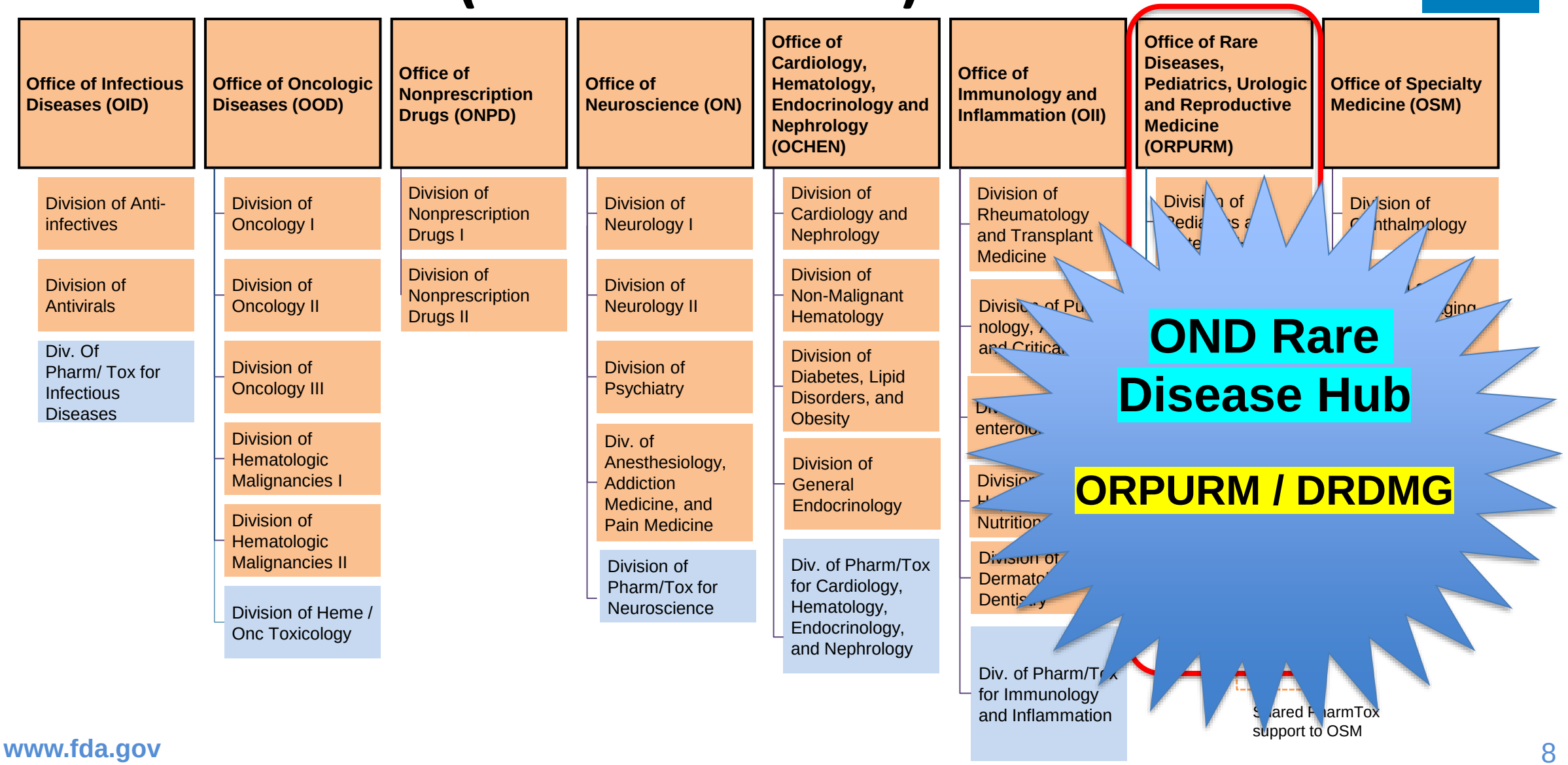


Division of Rare Diseases and Medical Genetics (DRDMG)

Rare Diseases Team:

Rare disease related cross – cutting programming, policy, education, and engagement

Inborn Errors Review Group:

Focuses on application-specific development work on Pre-INDs/INDs and NDAs/BLAs

CDER's Rare Diseases Team

- **Mission**: To facilitate, support, and accelerate the development of drugs and therapeutic biologics for rare diseases
- A multi-disciplinary team located in the Division of Rare Diseases and Medical Genetics in ORPURM
- Select activities:
  - Providing advice to other review divisions on their rare disease programs as requested
  - Promoting rare disease considerations across CDER's Office of New Drugs (OND)
  - Leading cross-cutting OND rare disease guidances, policies, strategic research, and workshops
  - Developing rare disease training and education
  - Engaging with internal and external stakeholders

Selected Rare Diseases Team Activities/Responsibilities

CDER's RDT Collaborates with Rare Disease Partners Across the FDA on these efforts

Draft Guidances

- Rare Diseases: Natural History Studies for Drug Development Link
- Rare Diseases: Common Issues in Drug Development Link

Programming

- International Rare Diseases Cluster with European Medicines Agency and Health Canada
- Rare Disease Drug Development Council
- PDUFA VI/VII rare disease commitments

Education

- Quarterly Rare Disease Seminar series
- Rare Disease Annual Reviewer Training Day

Engagement

- FDA/NIH Regulatory Fitness in Rare Disease Trials conference, May 16-17 2022
- Public meeting presentations for rare disease stakeholders (e.g. FDA Rare Disease Day)
- Rare Disease Patient Focused Drug Development meetings and Patient Listening Sessions
- Rare Disease Critical Path Innovation Meetings (CPIMs)

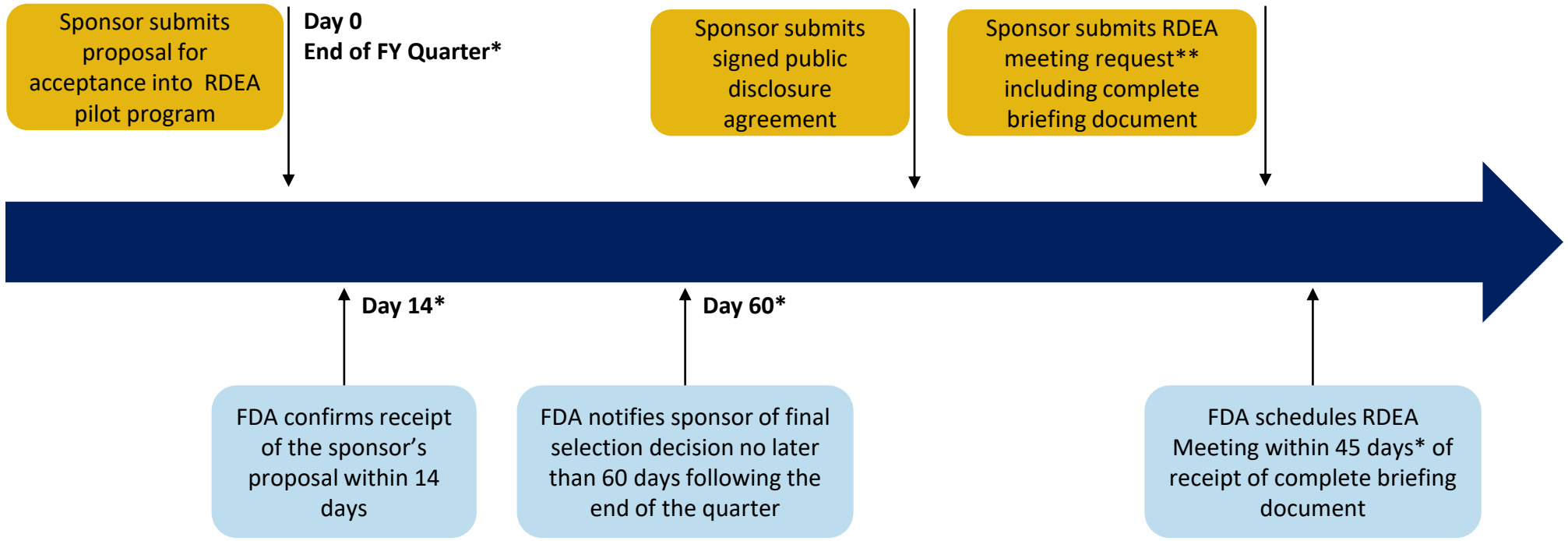
Rare **D**isease **E**ndpoint **A**dvancement Pilot Program Overview

- 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 Meeting Process and Timeline



**Timeframes denoted in PDUFA VII Commitment Letter*
***Sponsor may participate in up to four focused meetings as per the PDUFA VII Commitment Letter*

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.

Vision

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

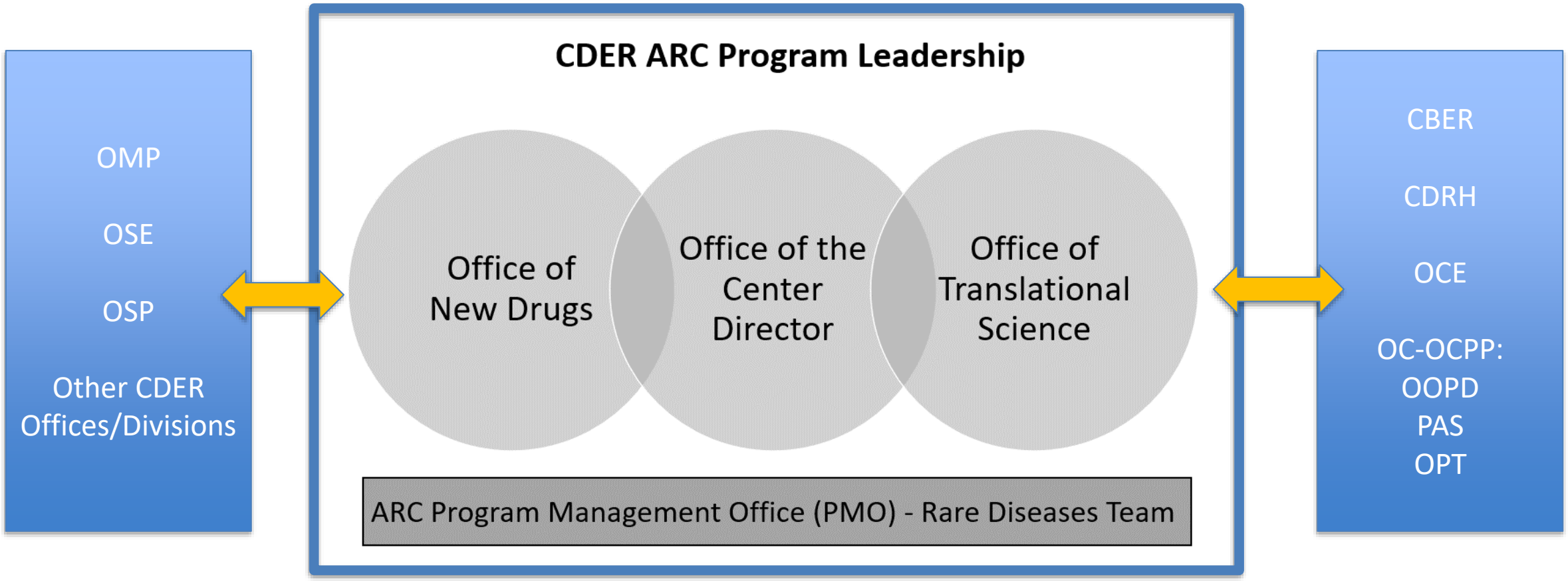
Mission

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.

Some Common Challenges in Rare Disease Drug Development

- Small and sometimes very **small patient populations**
- **Genotypic/phenotypic** heterogeneity within a disease
- **Natural history** often poorly understood
- Often **serious/life-threatening**, progressive, **childhood onset**
- Reluctance, at times, to randomize to placebo
- **Drug development tools** (e.g., established efficacy endpoints) often lacking
- Limited, if any, regulatory **precedent**
- Incorporating regulatory flexibility while upholding **regulatory standards**

CDER's ARC Program will work across FDA



CDER_ARC_Program@fda.hhs.gov

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

OMP=Office of Medical Policy, OSE=Office of Surveillance and Epidemiology, OSP=Office of Strategic Programs

CBER=Center for Biologics Evaluation and Research, CDRH=Centers for Devices and Radiological Health, OCE=Oncologic Center of Excellence, OC-OCPP=Office of the Commissioner: Office of Clinical Policy and Programs, OOPD-Office of Orphan Products Development, PAS=Patient Affairs Staff, OPT=Office of Pediatric Therapeutics

ARC YEAR 1: Focus on Engagement

Engagement in year 1 will inform CDER of stakeholder priorities and needs in rare disease drug development

- 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
  - 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 Meeting Link
- FDA and Duke Margolis Virtual Public Workshop: Translational Science in Drug Development: Surrogate Endpoints, Biomarkers, and More, May 24-25, 2022
  - Focus on translational science and the development of surrogate endpoints
  - Meeting link
- Patients & Patient Organizations
  - Patient Focused Drug Development staff to lead enhanced patient engagement through public workshops
    - CDER's Patient Focused Drug Development website
    - Email: PatientFocused@fda.hhs.gov

Conclusions

- In recent years, over 50% of CDER's novel drug approvals were for rare diseases
- The Rare Diseases Team in CDER works to facilitate, support, and accelerate the development of drugs and therapeutic biologics for rare diseases
- CDER collaborates with rare disease partners across the FDA to advance rare disease drug development
- In year 1, CDER's ARC program will help CDER work more effectively with our rare disease drug development partners

Challenge Question #1

- Looking at CDER novel drug approvals (2015-2021), 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