

CDER New Drugs Program: 2019 Update

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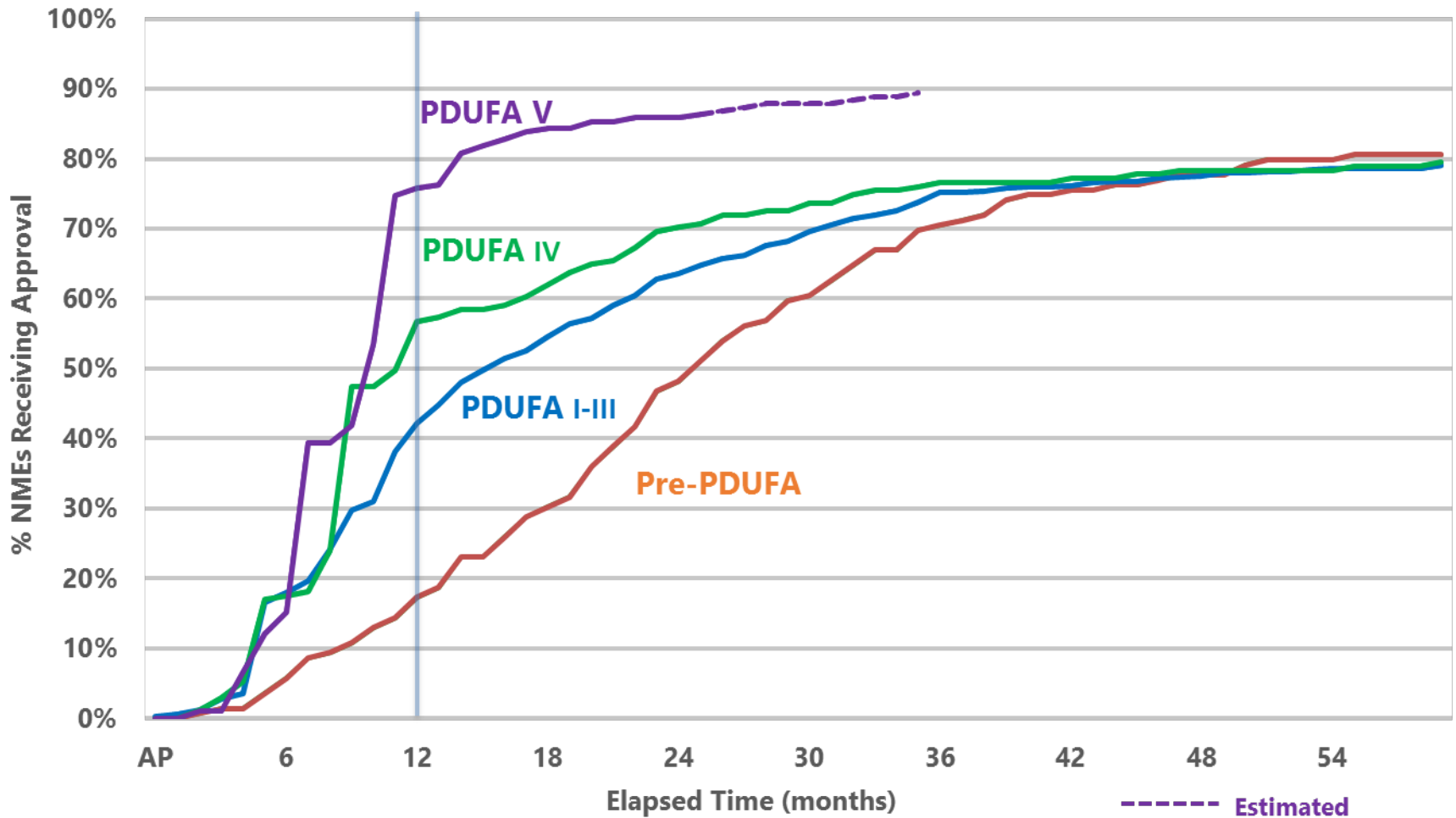
Housekeeping

- Data and analyses presented to reflect latest information, although usual QC for official FDA reports has not occurred. Presentation content should be considered *preliminary*.
- Pay close attention to fiscal year (FY), academic year (AY) and cut-off dates on data presentations; denominators are important too!
- Talented staff at FDA provide the data and analyses for this talk each year. Special thanks and acknowledgement to:
 - Nader Qassim, Nancy Maizel, and Reza Kazemi-Tabriz in CDER's Office of Program and Strategic Analysis
 - Mike Lanthier in the Office of the Commissioner

Topics to be covered

- New drug review process efficiency: a historical look and on-going changes in PDUFA VI
- New drug activity in 2019: approvals, workload, international comparisons, and profiling the 2019 class of NMEs/BLAs
- Development phase activity: IND workload, the breakthrough program, meeting workload and continued changes in PDUFA VI
- A look ahead to 2020: New Drugs Regulatory Program Modernization efforts

CDER New Molecular Entity Approval Rates by PDUFA Cohort



Projection estimates account for actions to date and elapsed time to date for non-approvals

New Drug Activity in 2019

- In FY 2019*, CDER has approved **45 NMEs**, including **23 orphan drugs**
 - **32 Priority Reviewed NME approvals**
 - **Roughly half of the NMEs** approved are orphan drugs to treat rare diseases
 - More than half of the orphans (12 of 23) are for cancer/cancer imaging
 - 4 for neuropsychiatric drugs for: LEMS, polyneuropathy of hereditary transthyretin-mediated amyloidosis, and two for excessive daytime sleepiness (EDS) in adult patients with narcolepsy
 - 3 orphans are for inherited genetic conditions: polyneuropathy of hereditary transthyretin-mediated amyloidosis, primary hemophagocytic lymphohistiocytosis (HLH), Adenosine Deaminase- Severe Combined Immunodeficiency (ADA-SCID)
- 2019 has a unique blend of therapeutic areas
- U.S. continues to lead the world in first approval of NMEs
- Several Notable Approvals, including:
 - **Trikafta**
 - **Recarbrio and Fetroja**
 - **Spravato**
 - **Scenesse**

* This information is accurate as of September 30th, 2019. In rare instances, it may be necessary for FDA to change a drug's new molecular entity (NME) designation or the status of its application as a new biologics license application (BLA). This note applies to all references to NME/Original BLAs in this presentation.

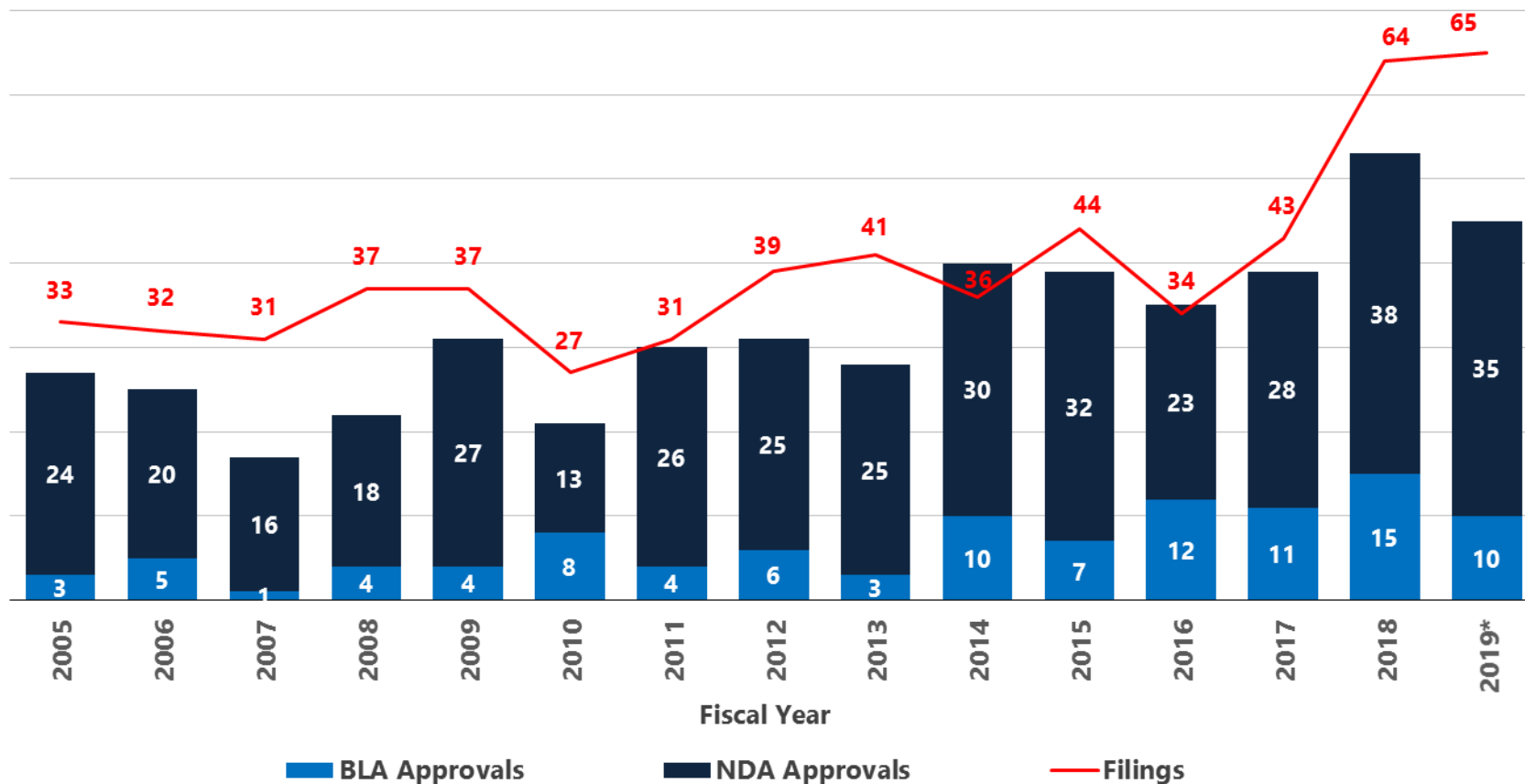
Notable Approvals: Not Only Quantity but Quality for 2019



- **Trikafta** - the first triple combination therapy to treat patients with Cystic Fibrosis (CF) who have the most common form of the CF gene mutation, which is estimated to represent 90 percent of the cystic fibrosis population for some patients with CF, but many patients have mutations that are ineligible for treatment.
- **Recarbrio and Fetroja** - two new antibiotics effective against certain Gram-negative infections --- important advances because Gram-negative bacteria represent a growing danger of serious and potentially life-threatening infections.
- **Spravato** - closely related chemically to the drug ketamine, originally approved in 1970 under the trade name Ketalar as an injectable anesthetic for certain diagnostic and surgical procedures. Esketamine was approved in 2019 as a nasal spray, to be used in conjunction with an oral antidepressant, for the treatment of depression in adults who have tried other antidepressant medicines but have not benefited from them (treatment-resistant depression).
- **Scenese** - to increase pain-free light exposure in patients with phototoxic reactions (sensitivity to sunlight) due to erythropoietic protoporphyria, a rare condition resulting from excess accumulation of a chemical that normally helps red blood cells deliver oxygen to the body

CDER NME NDAs/BLAs[†]

Filings and Approvals by FY as of 9/30/19

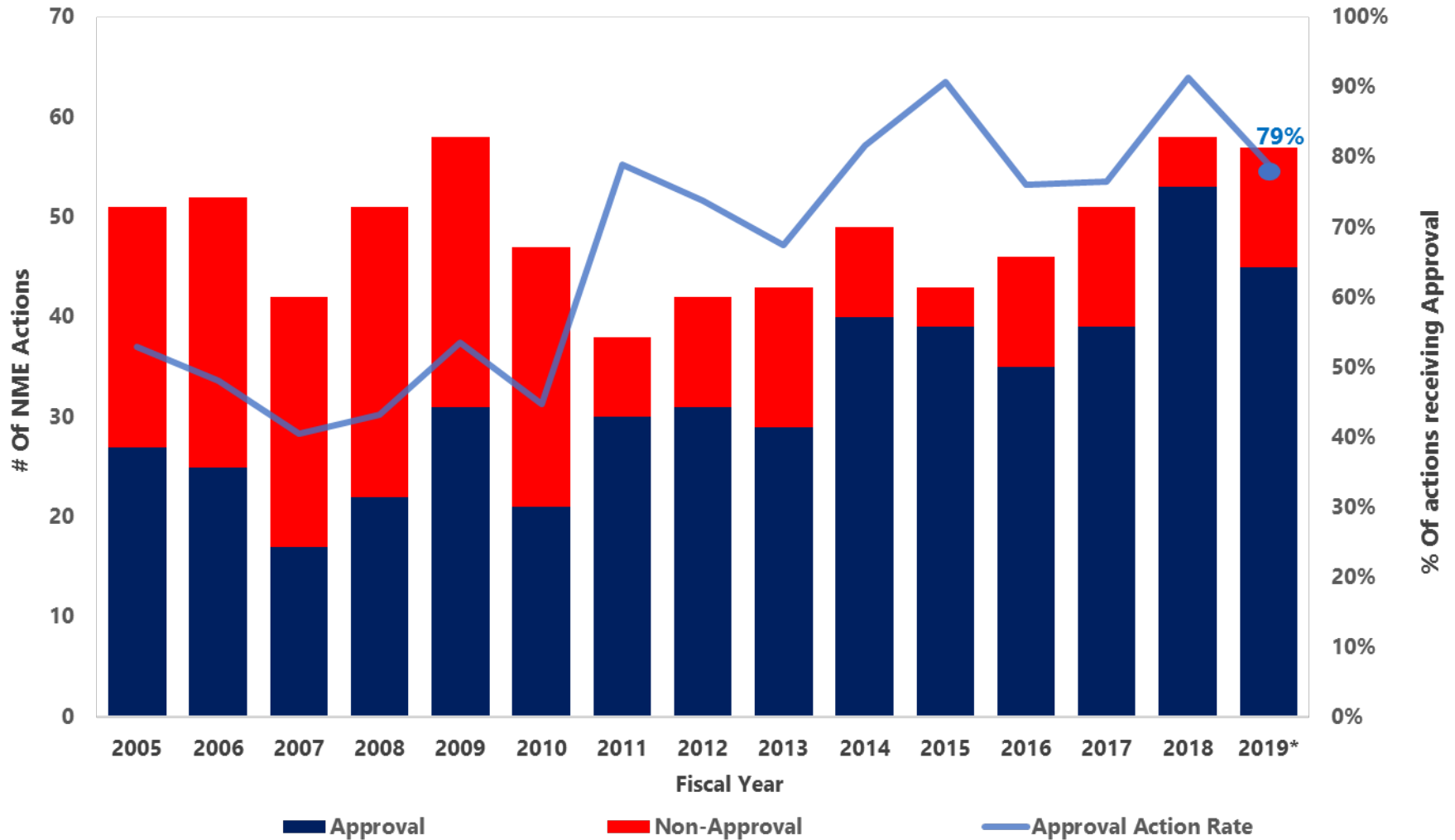


[†] Multiple applications pertaining to a single new molecular/biologic entity are only counted once. Original BLAs that do not contain a new active ingredient are excluded.

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Since applications are received and filed throughout a calendar year, the filed applications in a given calendar year do not necessarily correspond to an approval in the same calendar year. Certain applications are within their 60-day filing review period and may not be filed upon completion of the review.

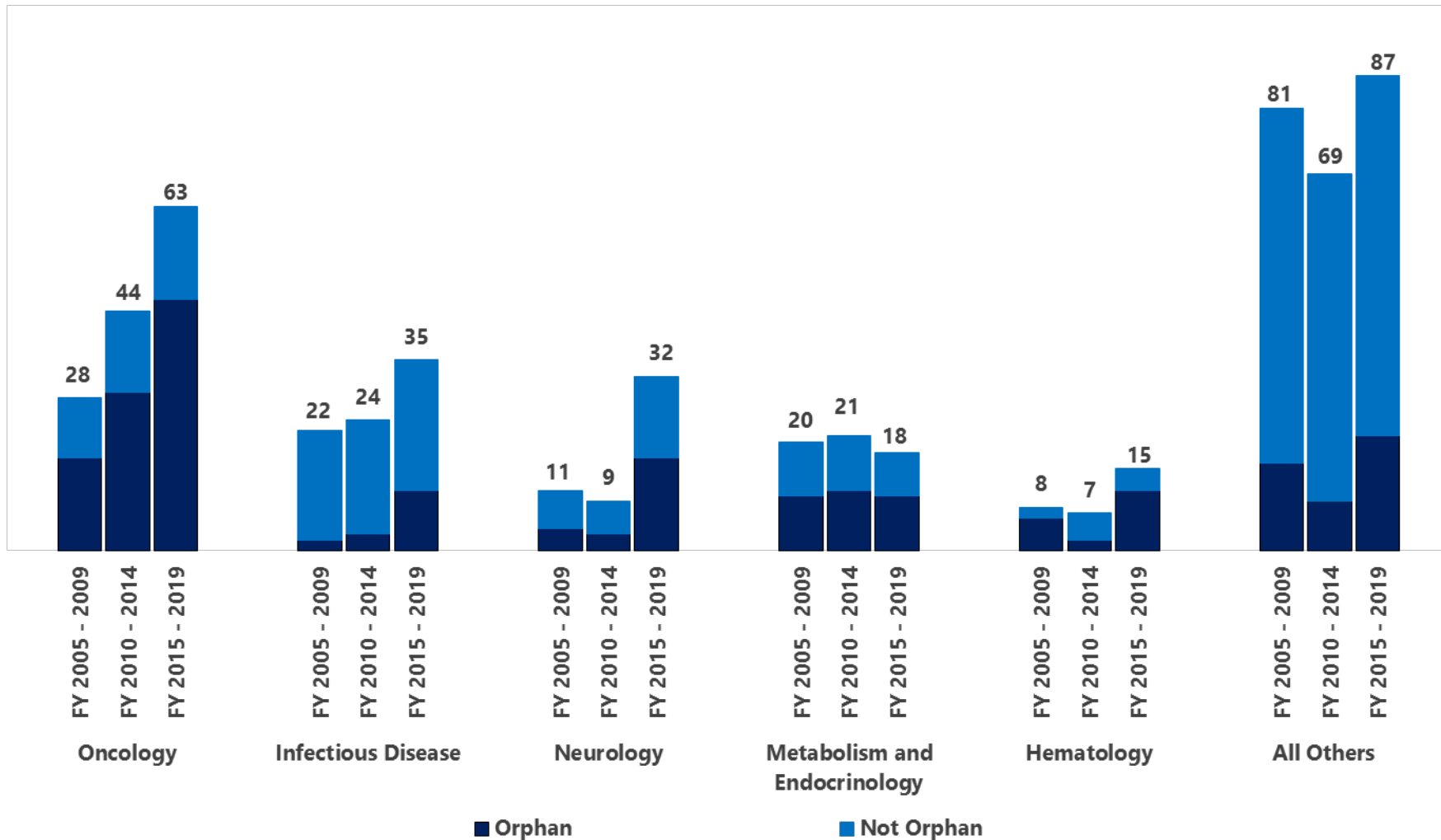
NME Actions and Approvals by FY



*Data as of 9/30/2019

Includes discrete actions on a given date for an active ingredient which, if approved, would constitute a new molecular entity. Actions for original submissions and resubmissions as well as actions for new BLAs are included. Multiple actions which occur on the same date for multiple dosage forms or indications are counted as a single regulatory action.

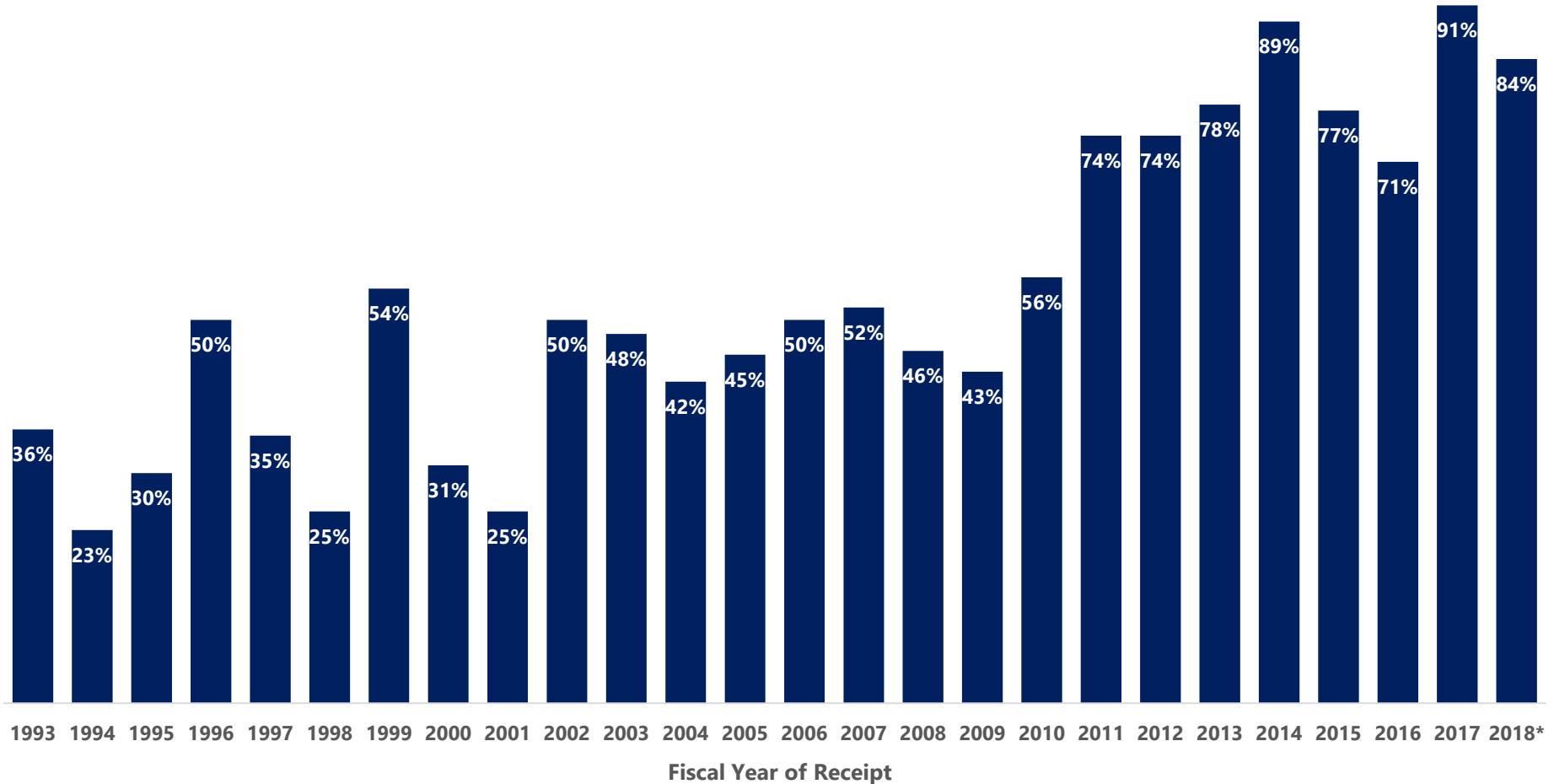
NME Filings by Fiscal Year and Therapeutic Area



* Data as of 9/30/2019

CDER NME NDAs/BLAs[†]

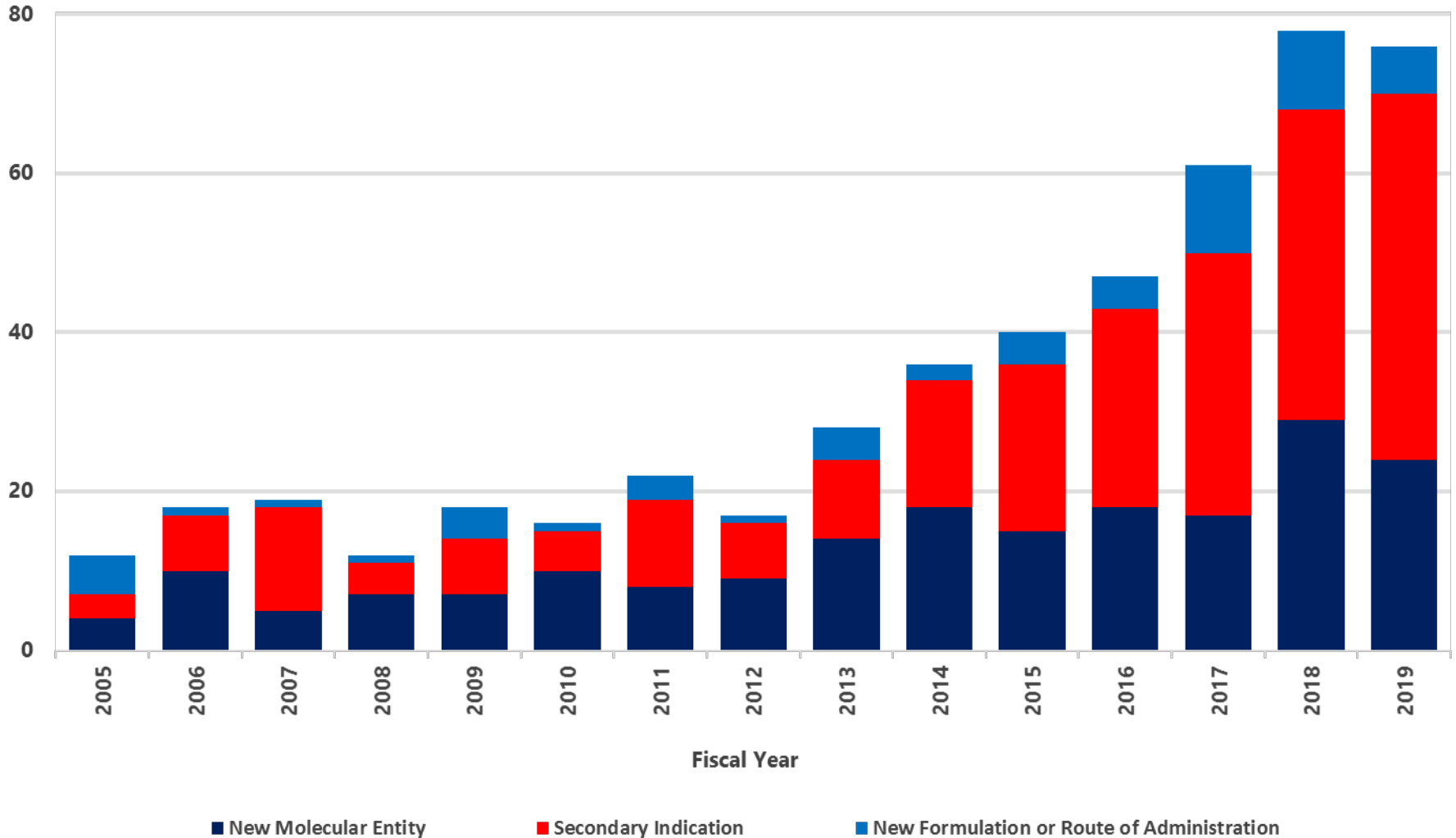
First Action Approval Rate by FY



* There are 3 Pending FY 18 applications as of 9/30/19

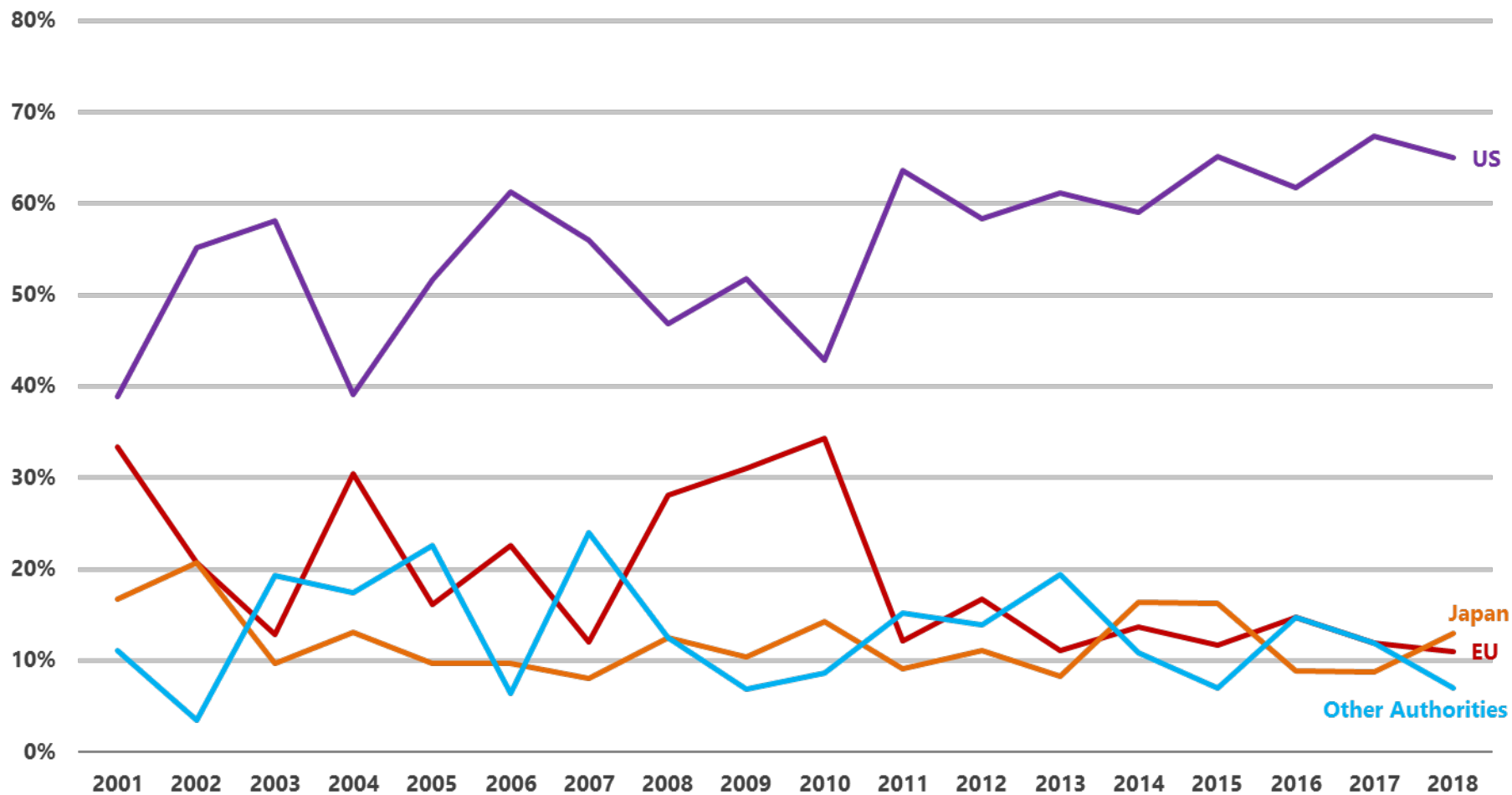
† Multiple applications pertaining to a single new molecular/biologic entity (e.g., single ingredient and combinations) are only counted once. Therefore, the numbers represented here for filings are not indicative of workload in the PDUFA V Program. Original BLAs that do not contain a new active ingredient are excluded.

CDER Orphan Drug Approvals by FY



* Data as of 9/30/2019

USA Share of New Active Substances Launched on World Market Remains High



Data as of 9/30/2019

Source: Scrip Magazine (1982 - 2006), Pharmaprojects/Citeline Pharma R&D Annual Review (2007 - 2018)

Snapshot of FY 2019



NME NDAs/BLAs[†] Drug Approvals (1/2)

Trade Name	Met PDUFA Goal Date*	Approved on First Cycle	First in Class	Approved First in the U.S.	Breakthrough Therapy	Priority Approval	Fast Track	Accelerated Approval	Orphan Drug	QIDP
SEYSARA	Green	Red		Dark Blue						
NUZYRA	Green	Red		Dark Blue		Orange	Light Green			Dark Blue
REVCovi	Green	Red		Dark Blue		Orange	Light Green		Yellow	
TEGSEDI	Green	Red	Light Blue			Orange	Light Green		Yellow	
TALZENNA	Green	Red		Dark Blue		Orange				
XOFLUZA	Green	Red	Light Blue			Orange				
LORBRENA	Green	Red			Blue	Orange		Light Orange	Yellow	
YUPELRI	Green	Red		Dark Blue						
AEMCOLO	Green	Red		Dark Blue		Orange	Light Green			Dark Blue
GAMIFANT	Green	Red	Light Blue	Dark Blue	Blue	Orange			Yellow	
DAURISMO	Green	Red		Dark Blue		Orange			Yellow	
VITRAKVI	Green	Red	Light Blue	Dark Blue	Blue	Orange		Light Orange	Yellow	
FIRDAPSE	Green	Red			Blue	Orange			Yellow	
XOSPATA	Green	Red				Orange	Light Green		Yellow	
MOTEGRITY	Green	Red								
ASPARLAS	Green	Red		Dark Blue					Yellow	
ULTOMIRIS	Green	Red		Dark Blue		Orange			Yellow	
ELZONRIS	Green	Red	Light Blue	Dark Blue	Blue	Orange			Yellow	
JEUVEAU	Green									
CABLIVI	Green	Red	Light Blue			Orange	Light Green		Yellow	
EGATEN	Green	Red				Orange	Light Green		Yellow	
ZULRESSO	Green	Red	Light Blue	Dark Blue	Blue	Orange				
SUNOSI	Green	Red		Dark Blue					Yellow	
MAYZENT	Green	Red		Dark Blue		Orange				

Data as of 9/30/2019

[†] Multiple submissions pertaining to a single new molecular/biologic entity (e.g., single ingredient and combinations) are only counted once. Therefore, the numbers are not indicative of workload in the PDUFA V Program. Original BLAs that do not contain a new active ingredient are excluded.

* A PDUFA Goal Date is marked as met if the NME is acted upon within its approval cycle due date.

Snapshot of FY 2019



NME NDAs/BLAs[†] Drug Approvals (2/2)

Trade Name	Met PDUFA Goal Date*	Approved on First Cycle	First in Class	Approved First in the U.S.	Breakthrough Therapy	Priority Approval	Fast Track	Accelerated Approval	Orphan Drug	QIDP
EVENTY	Green	White	Light Blue	Dark Blue	White	White	White	White	White	White
BALVERSA	Green	Red	Light Blue	Dark Blue	Blue	Orange	White	Orange	White	White
SKYRIZI	Green	Red	White	White	White	White	White	White	White	White
VYNDAQEL	Green	Red	Light Blue	White	Blue	Orange	Light Green	White	Yellow	White
PIQRAY	Green	Red	White	Dark Blue	White	Orange	White	White	White	White
POLIVY	Green	Red	Light Blue	Dark Blue	Blue	Orange	White	Orange	Yellow	White
VYLEESI	Green	Red	Light Blue	Dark Blue	White	White	White	White	White	White
XPOVIO	Green	Red	Light Blue	Dark Blue	White	Orange	Light Green	Orange	Yellow	White
RECARBRIO	Green	Red	White	Dark Blue	White	White	Light Green	White	White	Dark Blue
ACCRUFER	Green	Red	White	White	White	White	White	White	White	White
NUBEQA	Green	Red	White	Dark Blue	White	Orange	Light Green	White	White	White
TURALIO	Green	Red	Light Blue	Dark Blue	Blue	Orange	White	White	Yellow	White
<i>pretomanid</i>	Green	Red	Light Blue	Dark Blue	White	Orange	Light Green	White	Yellow	Dark Blue
WAKIX	Green	Red	Light Blue	White	White	Orange	Light Green	White	Yellow	White
ROZLYTREK	Green	Red	White	White	Blue	Orange	White	Orange	Yellow	White
INREBIC	Green	Red	White	Dark Blue	White	Orange	White	White	Yellow	White
RINVOQ	Green	Red	White	Dark Blue	White	Orange	White	White	White	White
XENLETA	Green	Red	White	Dark Blue	White	Orange	Light Green	White	White	Dark Blue
<i>GA 68 dotatoc</i>	Green	Red	White	White	White	White	White	White	Yellow	White
NOURIANZ	Green	White	Light Blue	White	White	White	White	White	White	White
IBSRELA	Green	Red	Light Blue	Dark Blue	White	White	White	White	White	White

Data as of 9/30/2019

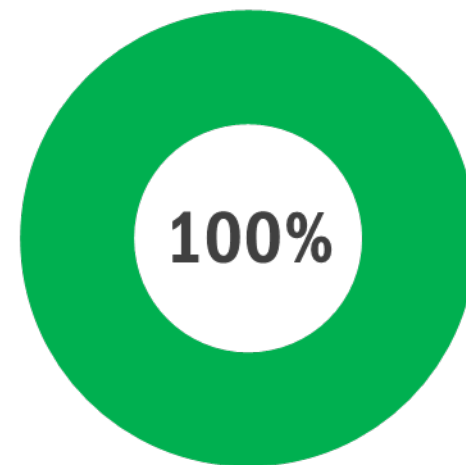
[†] Multiple submissions pertaining to a single new molecular/biologic entity (e.g., single ingredient and combinations) are only counted once. Therefore, the numbers are not indicative of workload in the PDUFA V Program. Original BLAs that do not contain a new active ingredient are excluded.

* A PDUFA Goal Date is marked as met if the NME is acted upon within its approval cycle due date.

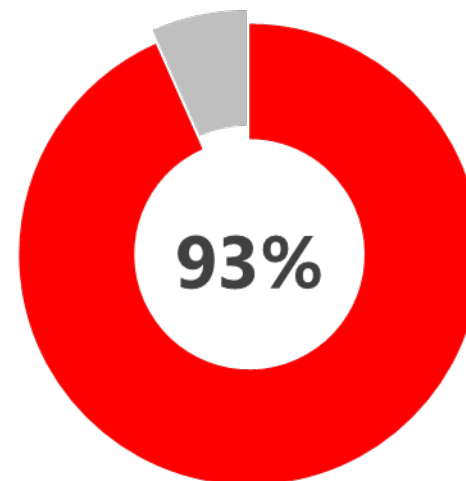
In FY 2019, CDER Continued To Ensure The Efficiency Of First Cycle Review

- All of the (100%) NMEs/BLAs approved in FY 2019 met their PDUFA goal dates
- All but three (93%) of the drugs approved in FY 2019 were approved in the first review cycle

Met PDUFA Goal Date



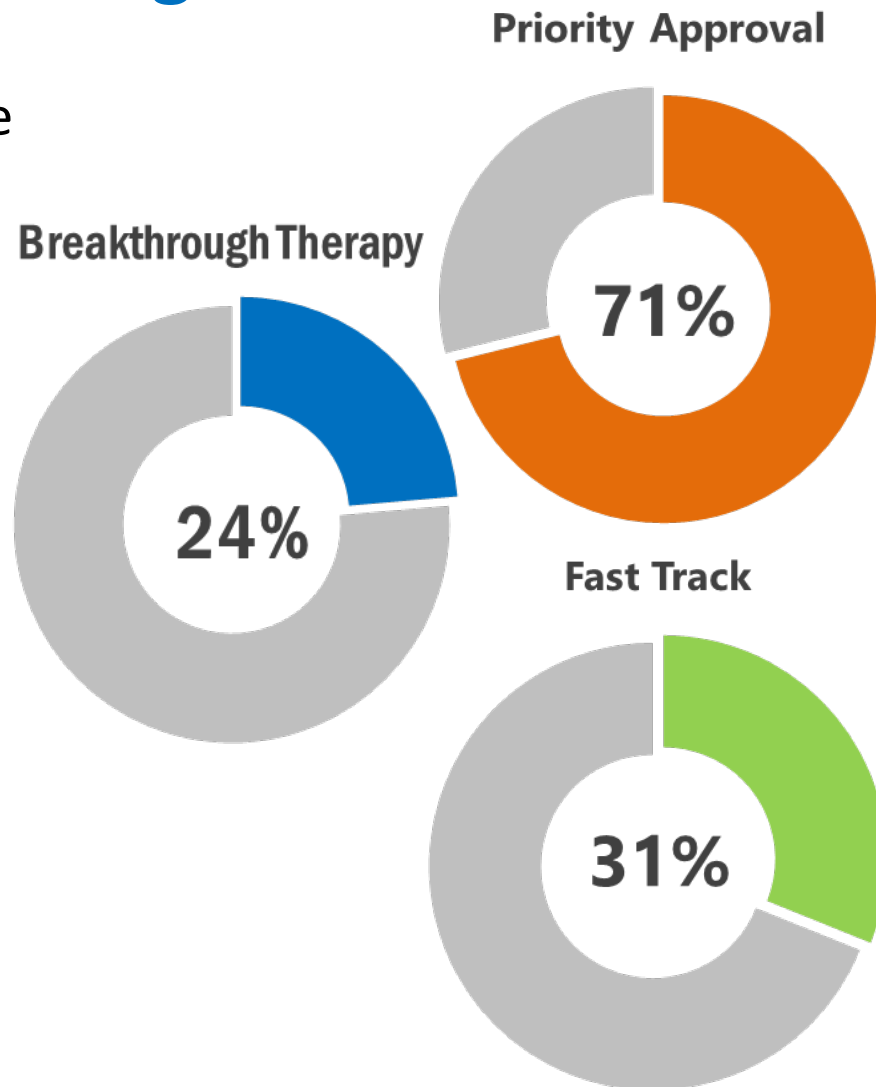
Approved on First Cycle



Utilization of Expedited Development and Review Programs Remained High in 2019



- Almost three – quarters (71%) of the drugs approved in FY 2019 were approved under Priority Review
- About one out of four (24%) of the drugs approved in FY 2019 received Breakthrough Therapy designation
- About three out of ten (31%) of the drugs approved in FY 2019 received Fast Track designation

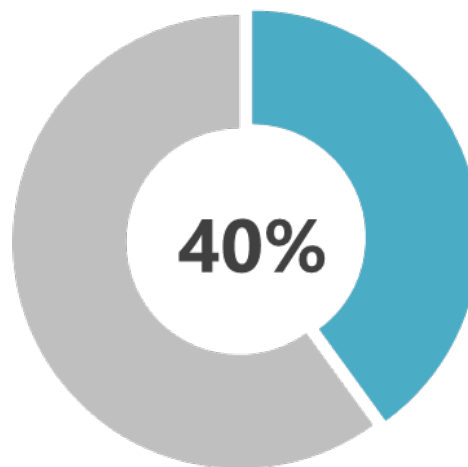


2019 Continues A Strong Track Record For Drug Innovation

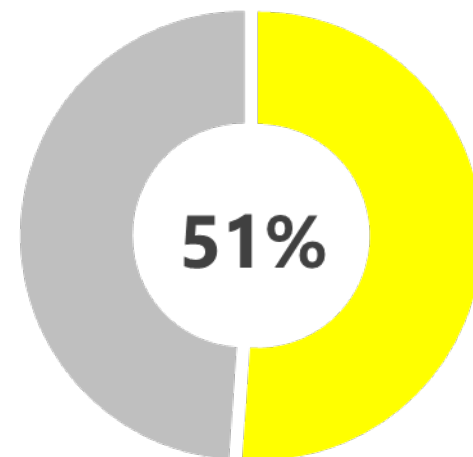


- Just over half (51%) of the drugs approved in FY 2019 are orphan drugs
- Four out of ten (40%) of the drugs approved in FY 2019 are the first in their class
- Almost two-thirds (64%) of the drugs approved in FY 2019 were first approved in the U.S.

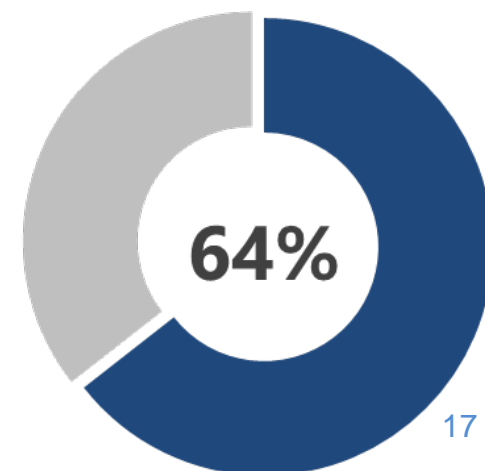
First in Class



Orphan Drugs



Approved First in the United States



Snapshot of FY 2020

NME NDAs/BLAs[†] Drug Approvals

13

NME

Approvals

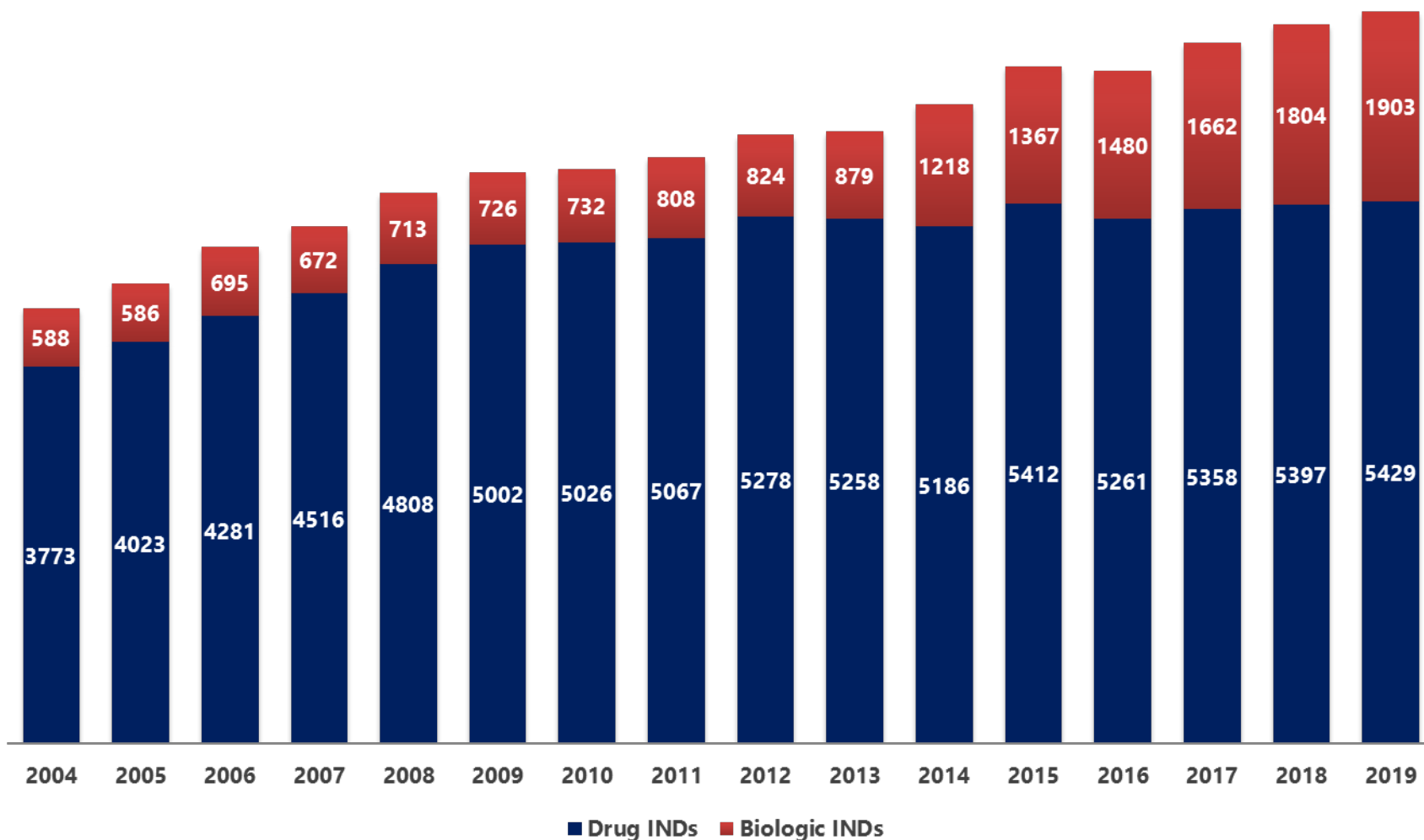
To date in FY 2020



Data as of 11/21/2019

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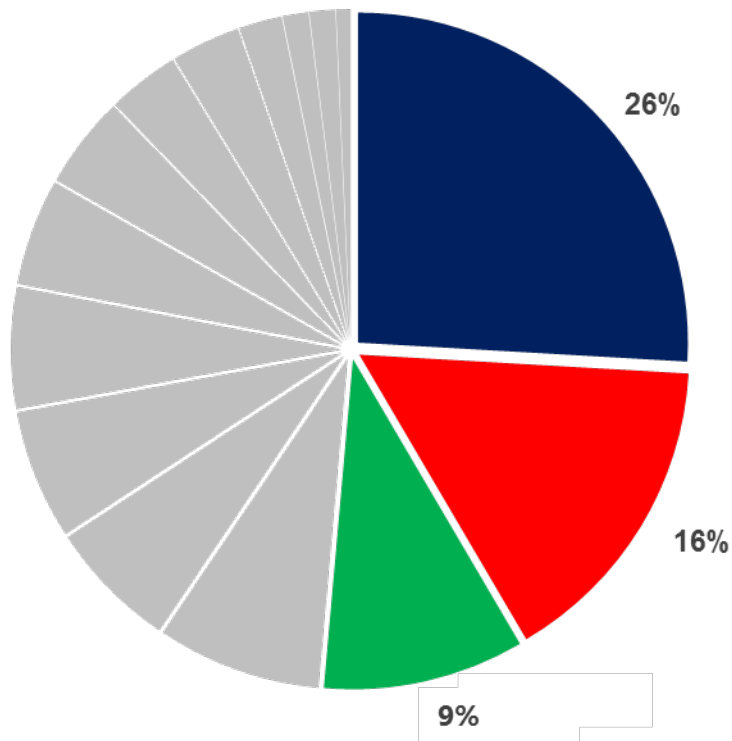
Development Phase Work Continued to Grow in 2019



Data are from the PDUFA Workload Adjuster and represent an Academic Year (12 month period of July 1st - June 30th)

CDER Breakthrough Therapy Requests by Division

Oncology, Hematology, and Neurology account for over 50% of Breakthrough Requests.



793 Requests since BT Program Inception in July 2012

Some notable conditions for FY 19 include

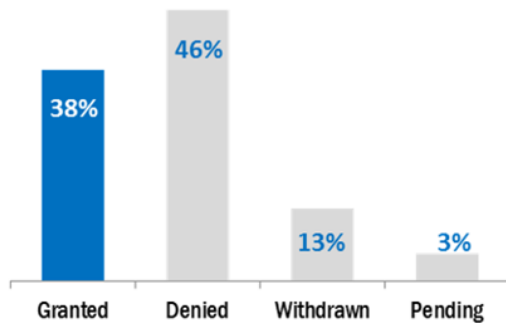
- Ebola Virus Disease
- Fragile X Syndrome (Cannabidiol)
- Chronic Hepatitis D

CDER Breakthrough Therapy Grants by Division

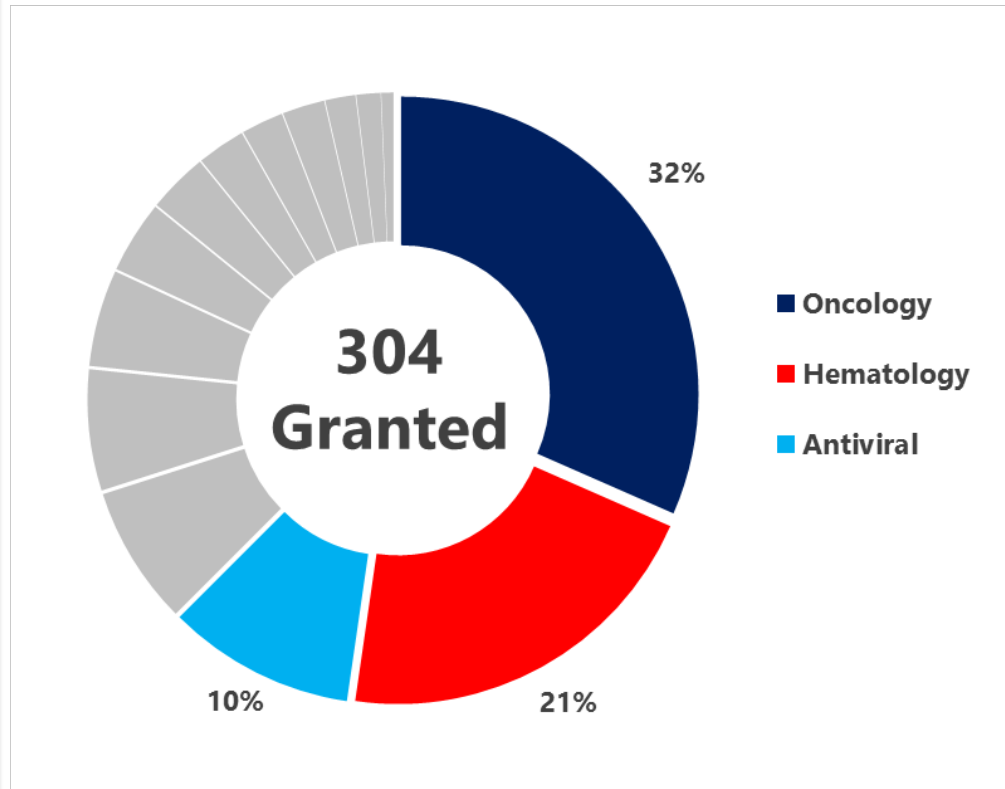
Of 793 BT Requests CDER issues a BT Grant about

38%

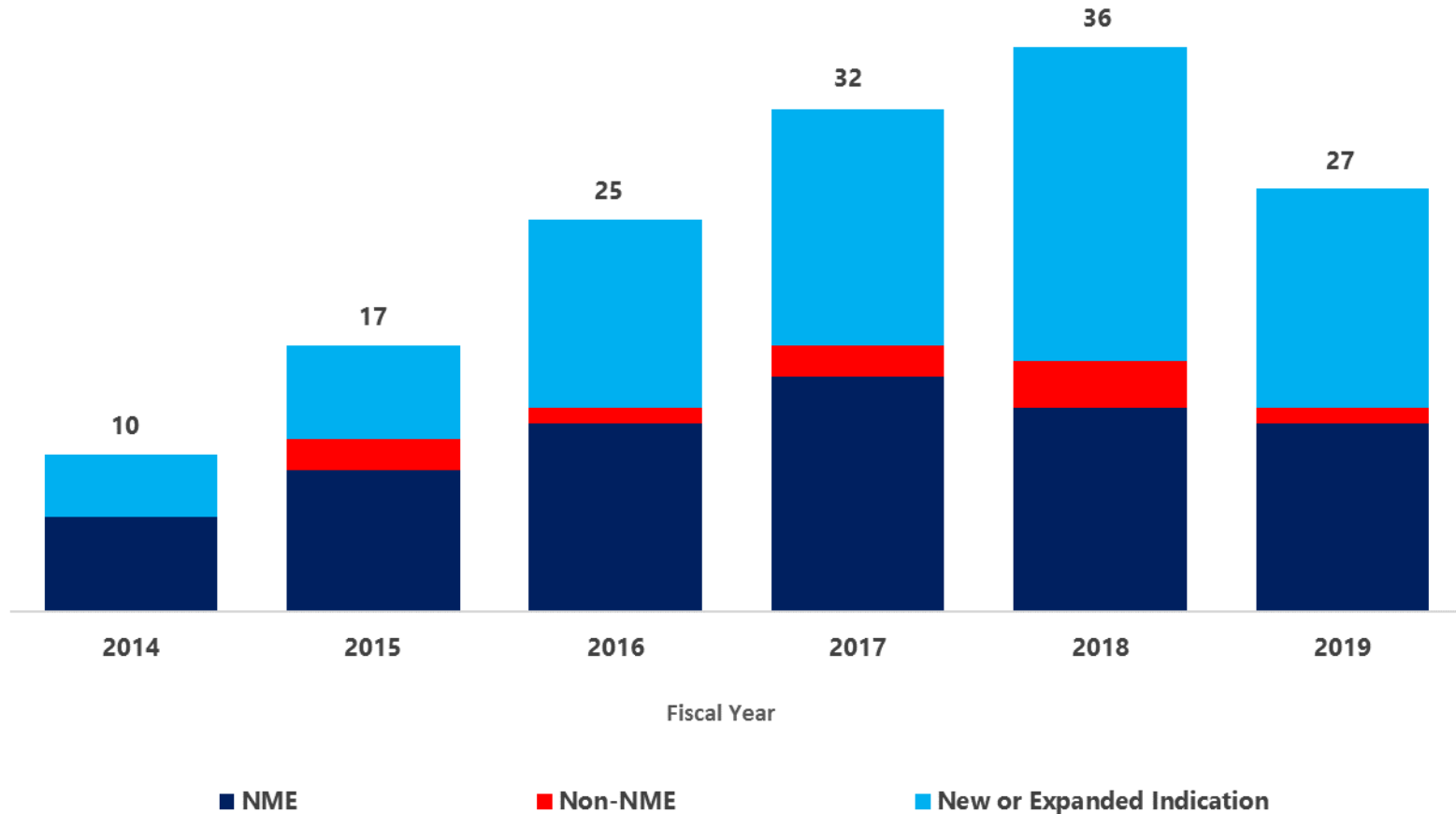
of the time



Oncology, Hematology, and Antiviral account for the majority of Breakthrough Grants

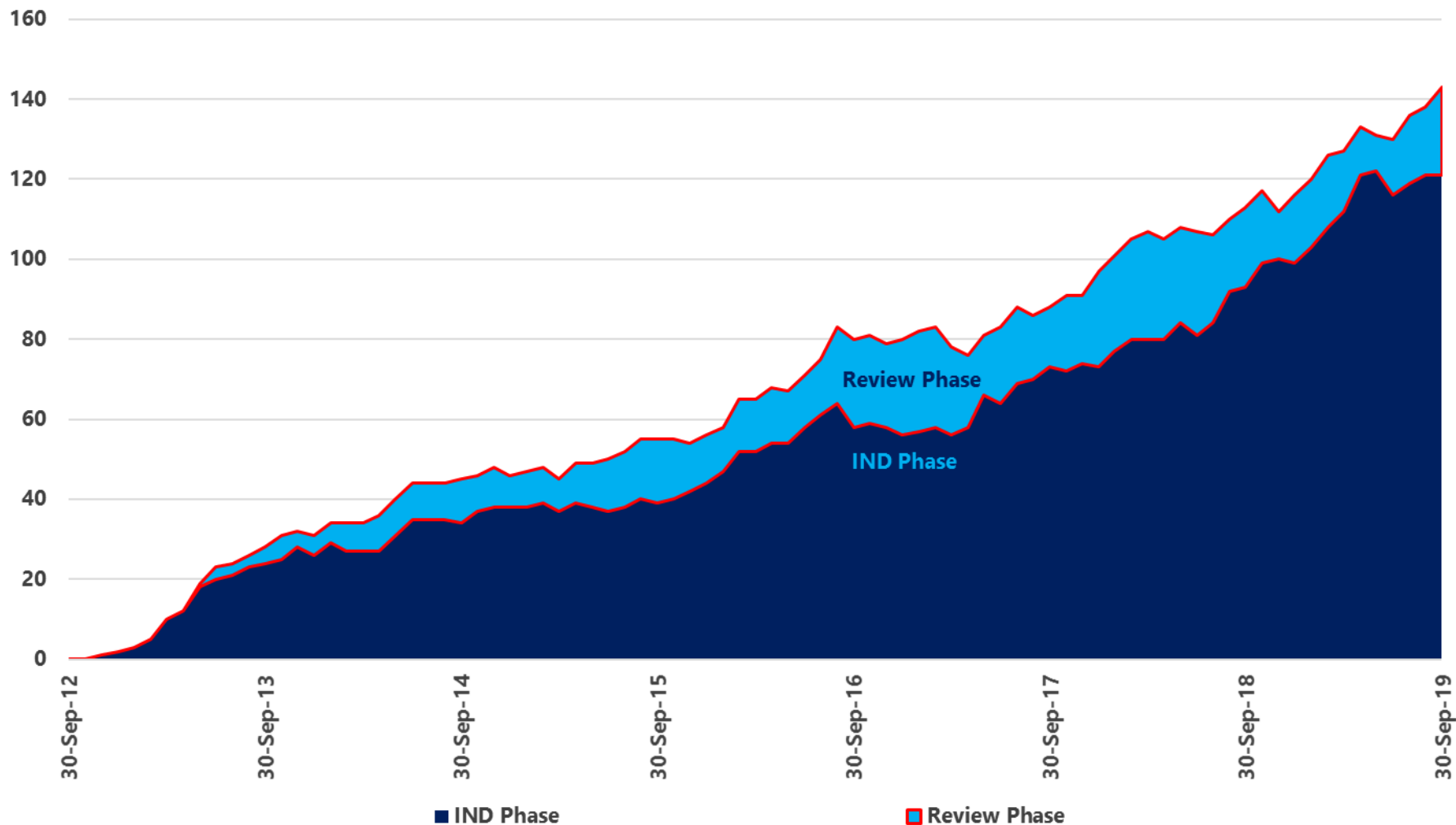


CDER Breakthrough Therapy Approvals by FY



* Data as of 9/30/2019

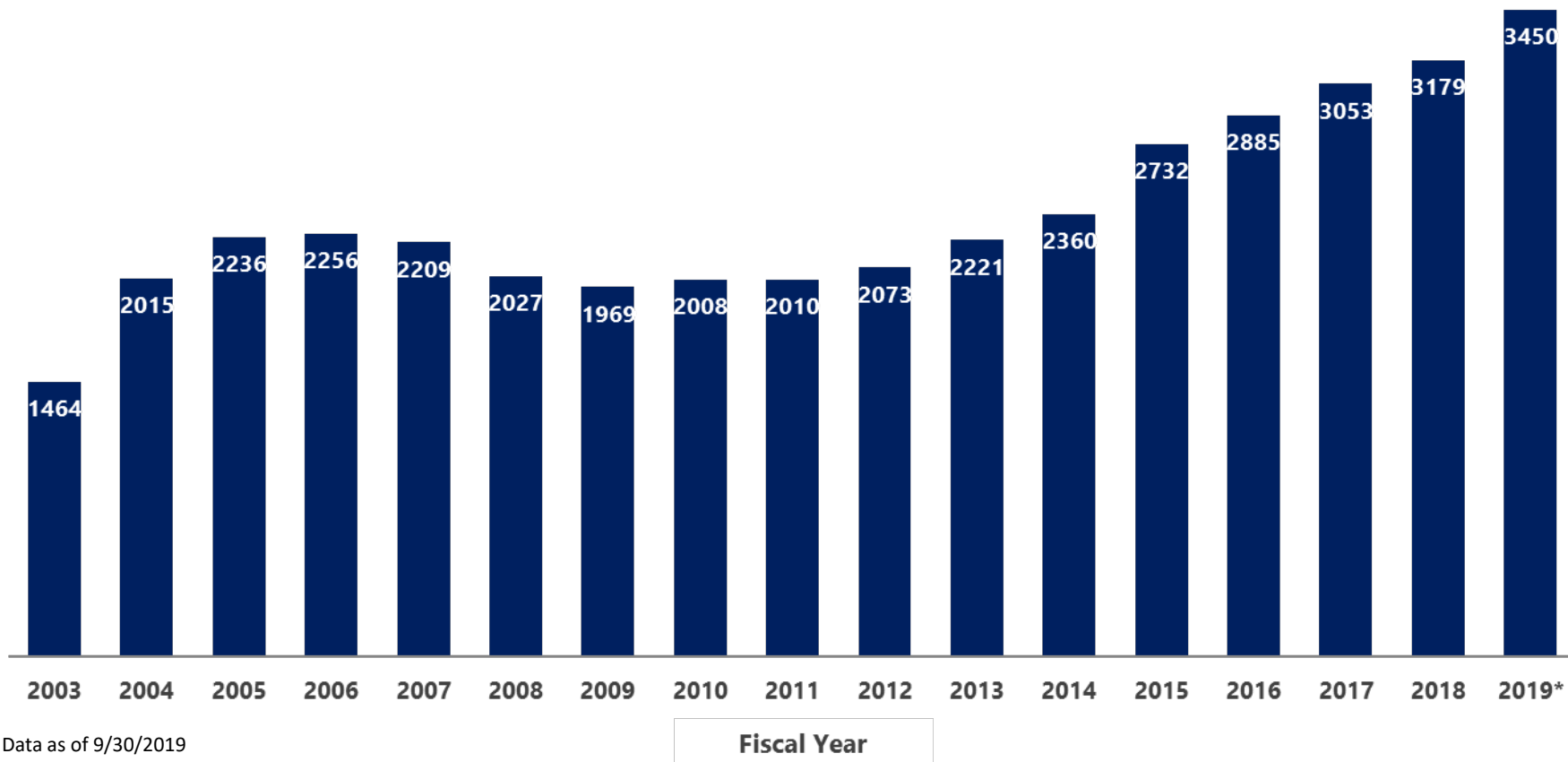
CDER Active Breakthrough Development Programs



* Data as of 9/30/19. Figures include total # of granted breakthrough designations for drug/indications under active IND development but have not yet received marketing approval or rescission decision.

CDER PDUFA

Formal Meeting Requests by FY

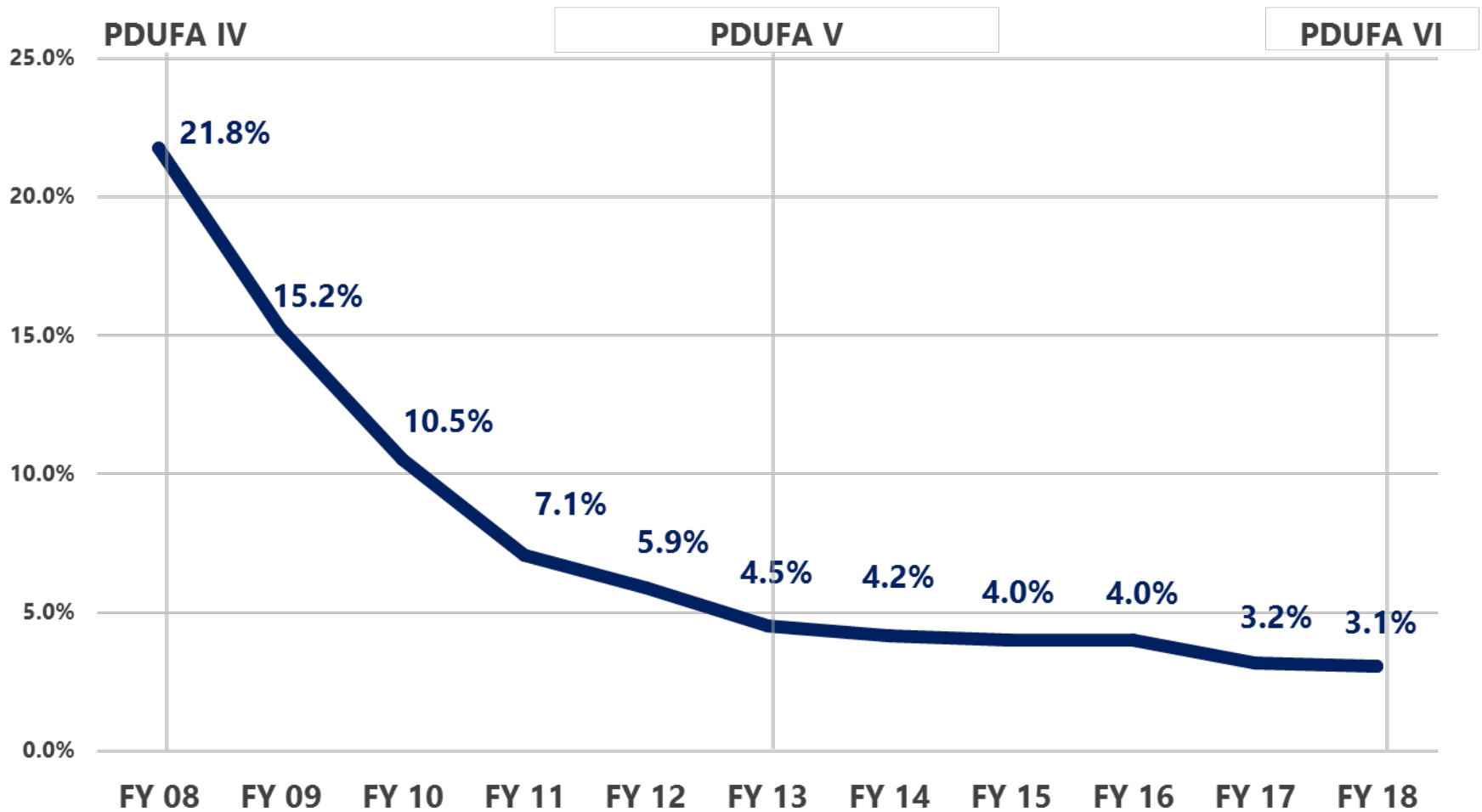


Data as of 9/30/2019

BLAs were transferred to CDER in FY2004

*2019 Data is preliminary

CDER Denied Meeting Requests By FY



Data as of 9/30/2019

New Drugs Regulatory Program Modernization

Objectives

Guiding principles for modernizing the new drugs regulatory program

Scientific Leadership

We will grow our scientific expertise and clarify pathways to regulatory approval.

- Expanding the armamentarium to address unmet medical needs is an important part of our public health mission.
- Towards that end, we will proactively collaborate with academic medical scientists and patient/disease advocates, evaluate scientific gaps, and strategically foster drug development.

Integrated Assessment

We will critically, collaboratively and consistently assess whether information in submissions meets statutory and regulatory requirements.

- We will take a new approach to document our assessments, developing a more integrated, cross-disciplinary document to foster collaboration and reduce redundant information.
- Our assessments will be rigorous, risk-based, and clinically relevant; focus on the key issues; and incorporate the patient perspective.

Benefit-Risk Monitoring

We will establish a unified post-market safety surveillance framework.

- To effectively protect the American public, we will systematically monitor the benefits and risks of approved drugs across their lifecycles.

Managing Talent

We will attract, develop, and retain outstanding people.

- We will use 21st Century Cures Act authorities to recruit and retain technical, scientific and professional experts, and eliminate our backlog of vacant positions.

Operational Excellence

We will have a dedicated focus on operational excellence.

- We will enhance our ability to address OND's large volume workload through greater process standardization and better defined roles and responsibilities.
- This will improve operational efficiency and enable our scientists to focus on science, not ancillary tasks.

Knowledge Management

We will facilitate knowledge management.

- Vast and diverse information is submitted to and generated by the New Drugs Regulatory Program.
- We will make it easy for our staff to find and use scientific and regulatory precedents.
- This will reduce manual work time, increase the speed and efficiency of submission assessment, and increase the consistency and predictability of regulatory decision-making.

The New Drugs Regulatory Program has 6 active initiatives

Integrated Review for Marketing Applications

Developing a streamlined interdisciplinary review process and template to support the new integrated review for assessing NDA/BLAs

IND Review Management

Streamlining the IND scientific review processes for managing IND applications, beginning with 30-Day Safety Reviews and Protocols

Post-Market Safety Management

Creating a standardized, consistent, and effective approach to post-market drug safety

Assessing Talent

Developing an effective and consistent process for hiring, onboarding, developing and evaluating new Clinical and Pharm/Tox reviewers

Reorganization and Transition Management

Planning, coordinating, and implementing modernization and organization changes at the future Office and Division levels across the New Drugs Program

Administrative Operations

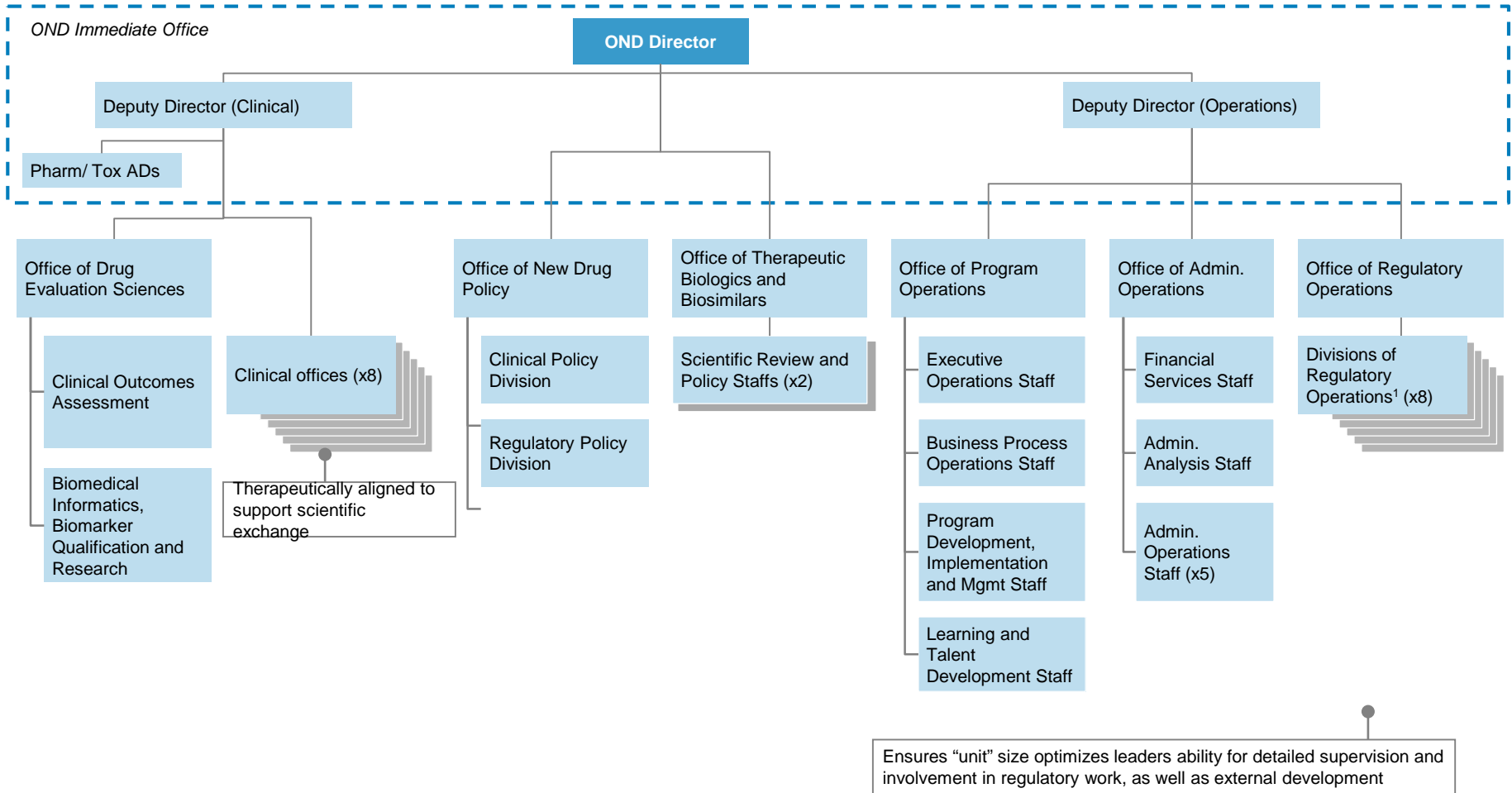
Optimize administrative and clerical staff roles, structure, and functions to enhance customer focus and employee engagement

Re-org will therapeutically align offices and divisions to support scientific exchange and improve consistency across OND



Approved

Details to follow



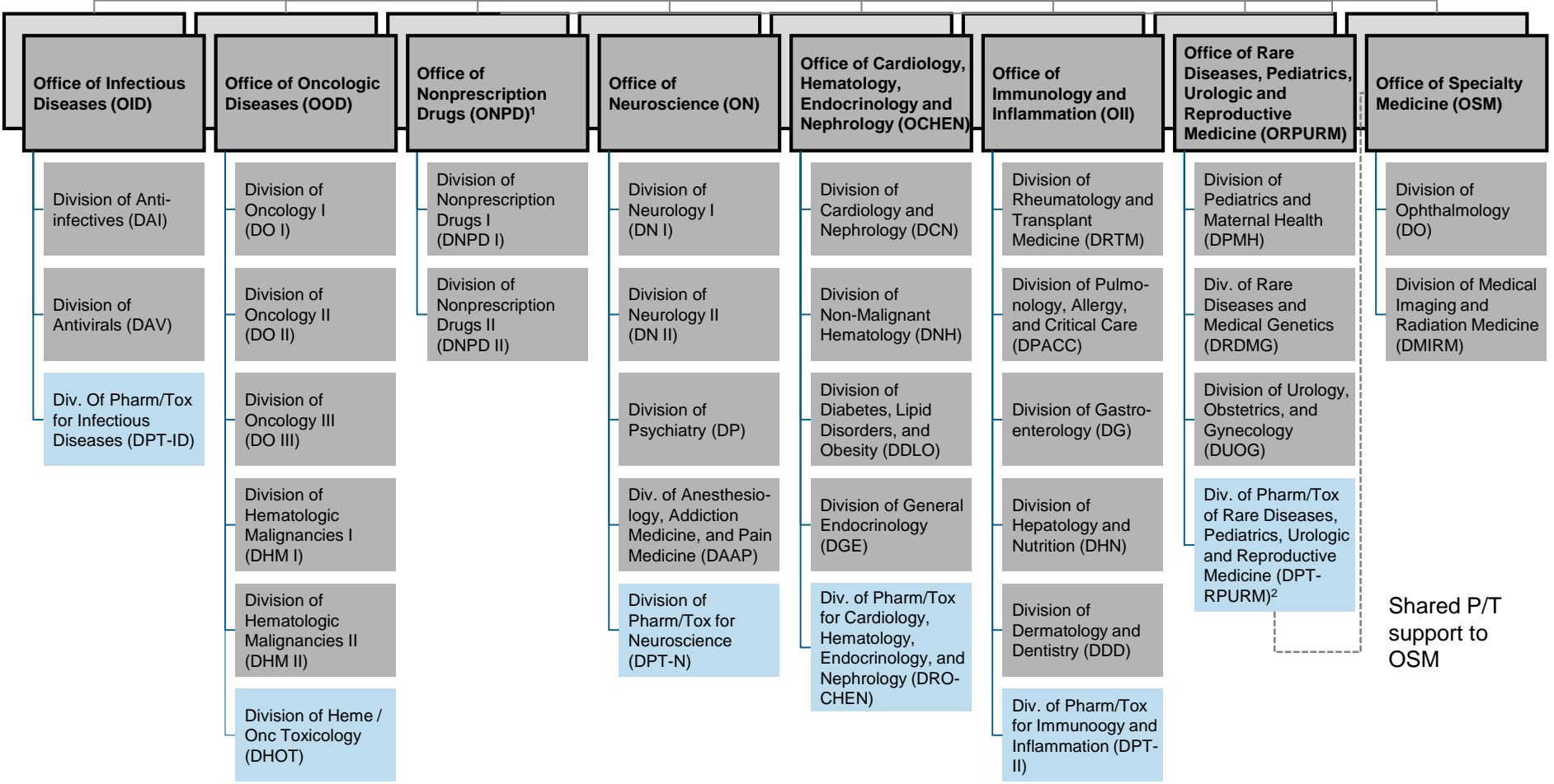
1 Regulatory Operations Divisions align to each clinical office

Clinical Office and Division Names



Approved

Office of Regulatory Operation: Divisions of Regulatory Operations



Shared P/T support to OSM

¹ ONPD P/T staff in the ONPD IO given the small current size of P/T staff. P/T staff will grow into a division from OMUFA;

² Single P/T division with staff supporting both ORPURM and OSM; PT DD will have dotted line reporting to ORPURM and OSM for P/T issues, and solid line to ORPURM Office Director for PMAP, etc.

Integrated Review of Marketing Applications

- Effort attempts to design a streamlined issue-based integrated review process and template that reduces silo reviews, by
 - Creating **a template and a process** that are issue-based, foster interdisciplinary collaboration, reduce redundancy and low-value work, and enable better knowledge management
 - Developing a **tracking tool** to be utilized from pre-NDA through end of review cycle, allowing for systematic tracking of review issues for the entire review team
 - Adding **new roles** to allow reviewers to focus on the science and regulatory aspects of the application: (1) Clinical Data Scientists to support safety analysis and (2) Medical Editors to provide editing and formatting services
 - Incorporating **purposeful scoping working meetings** with early involvement of leadership to discuss known benefit and risk issues; and **joint assessment meetings** focused on specific review issues

Currently in Phased Implementation. All divisions to begin using the new process and template in 2020.

IND Review Management

- Effort attempts to address variable practices across divisions and reduce redundant documentation practices
- Creating templates that are **issue-based**, foster **interdisciplinary collaboration**, **reduce redundancy** and low-value work, and enable better **knowledge management**
- Establishing procedures that **standardize** the review process, clearly **define roles and responsibilities** and improve our ability to provide **high-quality feedback** to sponsors in a **timely manner**
- Developing a risk based approach to **categorize** incoming protocols and amendments and identify the protocols that should follow a **higher priority process** to review more expeditiously

Currently in Phased Implementation. All divisions to begin using the new process and template in 2020.

Post-Market Safety Management

Create a **standardized** post-market drug safety framework that will include:

- **Cross-disciplinary, collaborative, science-focused** assessments
- Clear **roles, responsibilities, and governance**
- IT-enabled processes to enhance **knowledge management** and fit-for-purpose **analytic tools** to promote optimal evaluations
- **Policies and processes** (i.e., via SOPs, charters, templates) that support this framework

Anticipate beginning implementation in 2020

