

CDER New Drugs Program: 2017 Update

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FDA/CMS Summit
December 5th, 2017



Housekeeping

- Data and analyses presented 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), calendar year (CY), or 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

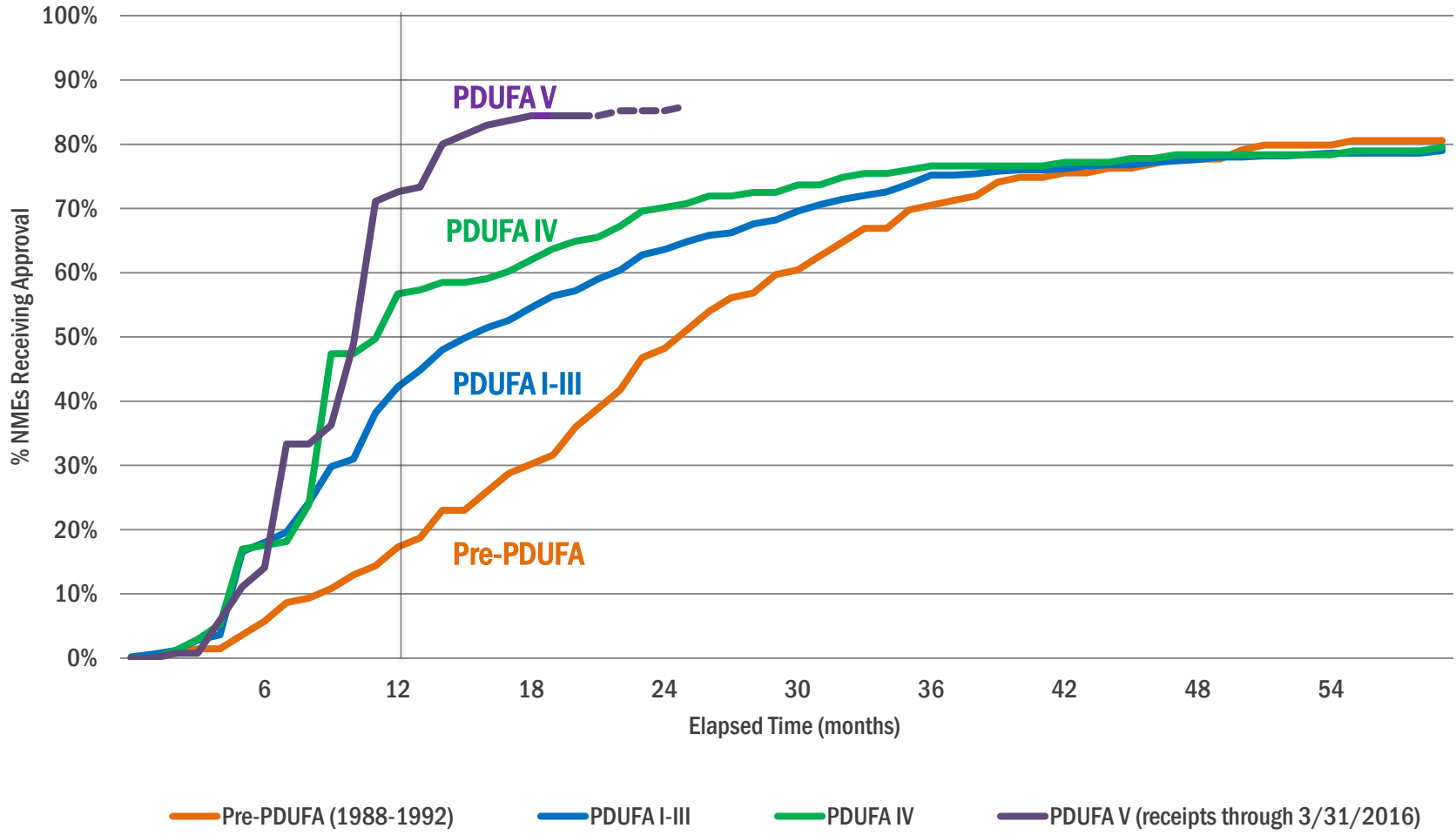


Topics to be covered

- New drug review process efficiency: a historical look and changes in PDUFA VI
- New drug activity in 2017: approvals, workload, international comparisons, and profiling the 2017 class of NMEs/BLAs
- Development phase activity: IND workload, the breakthrough program, meeting workload and changes in PDUFA VI
- A look ahead to 2018



CDER New Molecular Entity Approval Rates by PDUFA Cohort



* PDUFA V estimates based on 77 NMEs submitted in FY 2013 – mid FY 2015 (it is too early to estimate performance for later submissions)
 Projection estimates account for actions to date and elapsed time to date for non-approvals



NME Review Program

- PDUFA V established a new review model for NME NDAs and original BLAs that had three main features:
 - Specified touchpoints during review for FDA-applicant communication [i.e., mid-cycle communication, late-cycle meeting (LCM)]
 - Additional time for FDA review
 - Independent contractor (Eastern Research Group) evaluations
- Highly successful program – a conclusion shared by industry, FDA, and ERG
- Changes in PDUFA VI
 - Flexibility: FDA and applicant may agree on a Formal Communication Plan; codified treatment of expedited reviews; LCMs may be held by phone rather than F2F
 - Application orientation meetings are envisioned as part of a communication plan
 - Advisory committee meetings may be scheduled slightly later in the review process; FDA and applicant have option for informal teleconference to debrief on AC feedback
- Review Program is now applied to biosimilar applications in BsUFA II



New Drug Activity in 2017

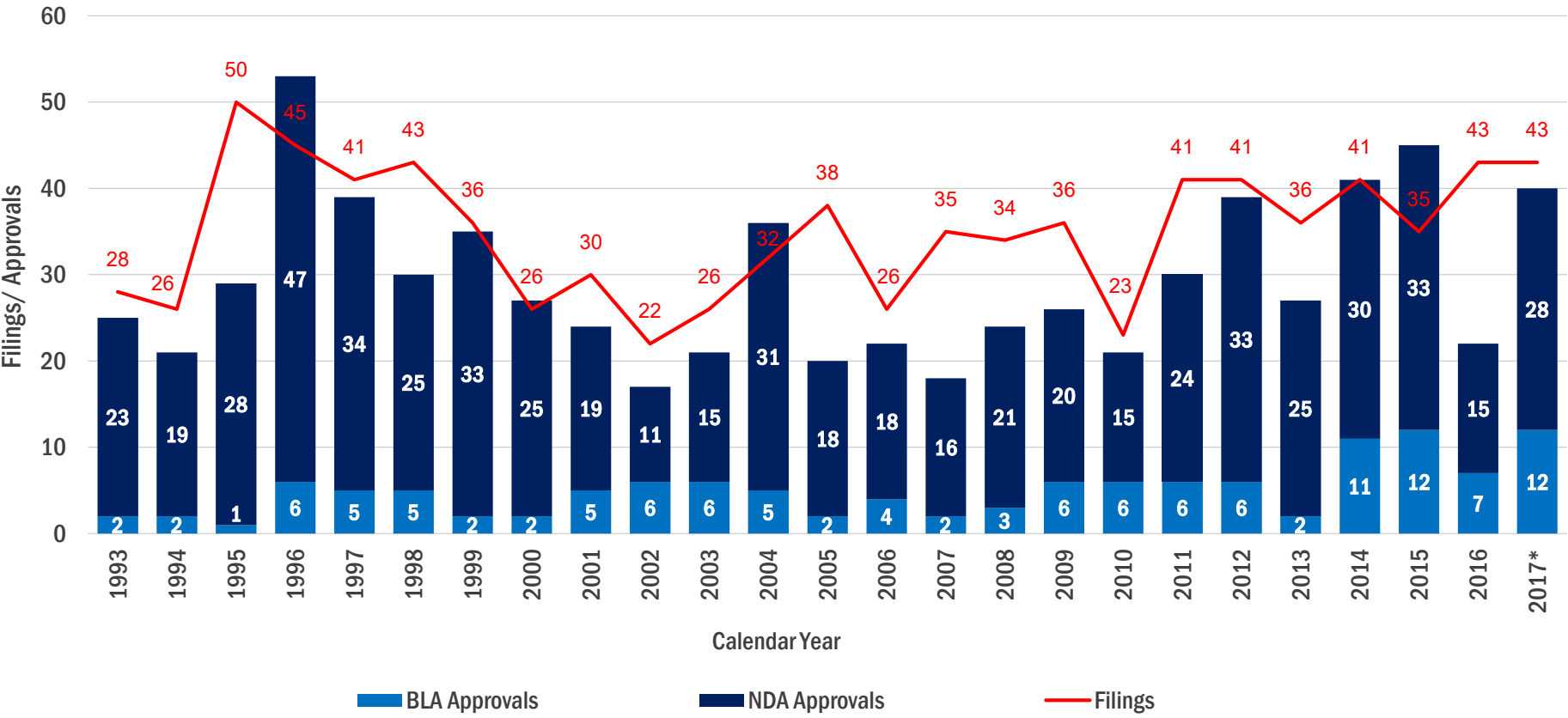
- In CY 2017 so far*, CDER has approved 40 NMEs, including 17 orphan drugs
 - Record number of orphan indications approved across all NDAs and BLAs (not just NMEs and BLAs)
 - US continues to lead the world in first approval of NMEs
- In FY 2017, new applications increased across the board for CDER compared to five year averages:
 - 48 NMEs and original BLAs (14% increase)
 - 106 non-NME NDAs (28% increase)
 - 231 efficacy supplements (43% increase)

* This information is accurate as of November 30th, 2017. 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.



CDER NME NDAs/BLAs[†]

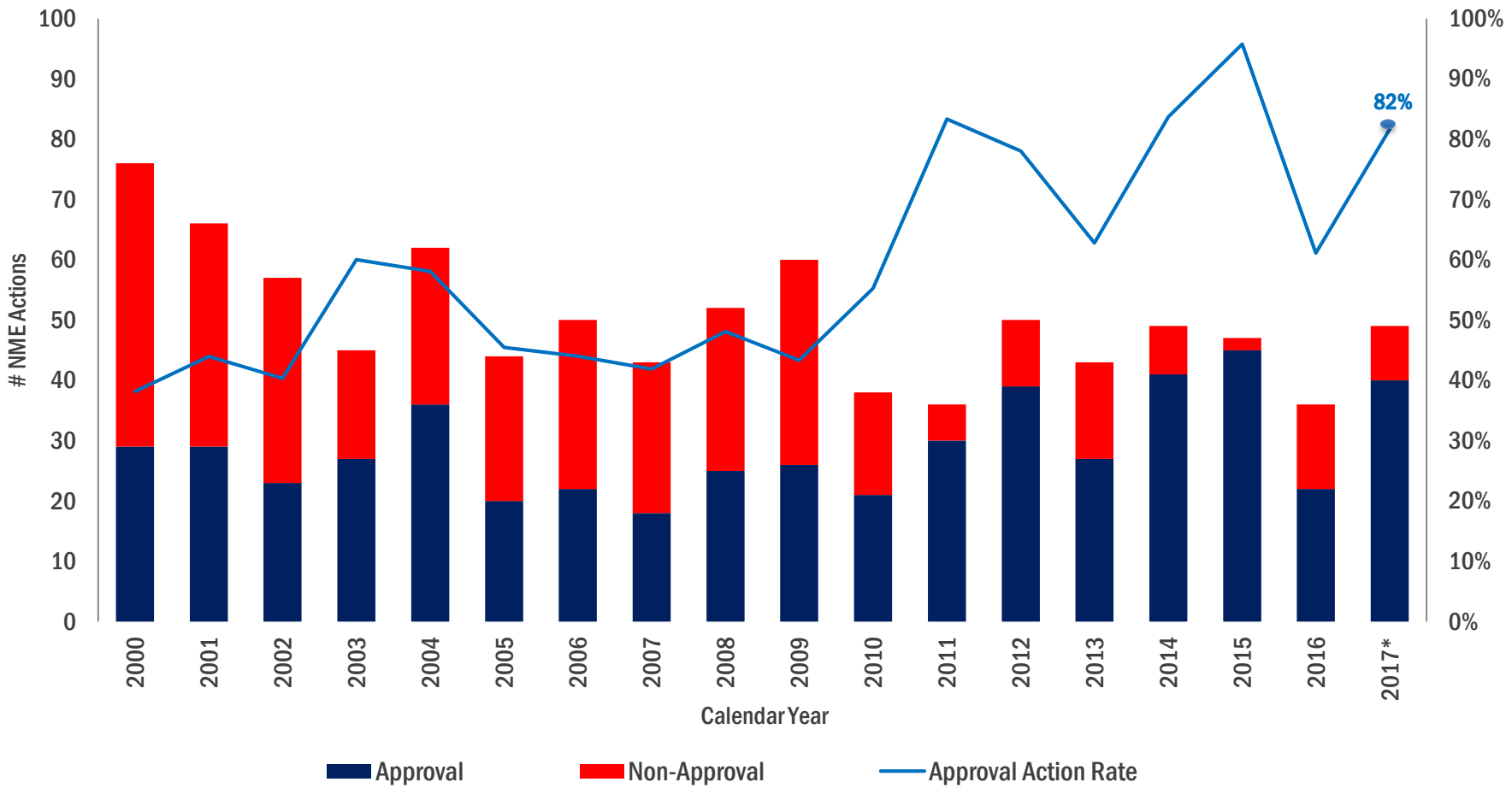
Filings and Approvals by CY as of 11/30/17



[†] 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.
 * This information is accurate as of November 30th, 2017. 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.
 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 CY



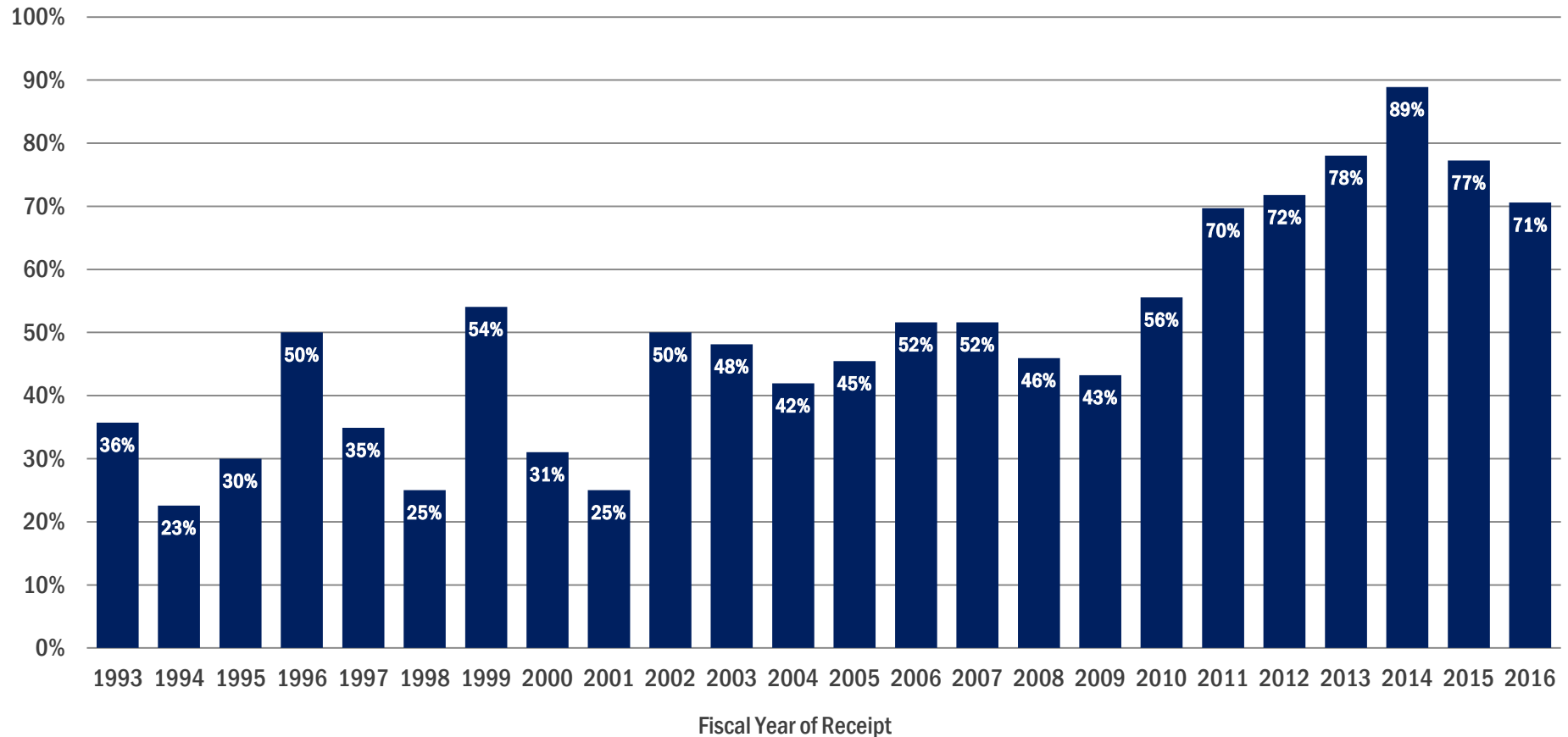
*Data as of 11/30/2017

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.



CDER NME NDAs/BLAs[†]

First Action Approval Rate by FY

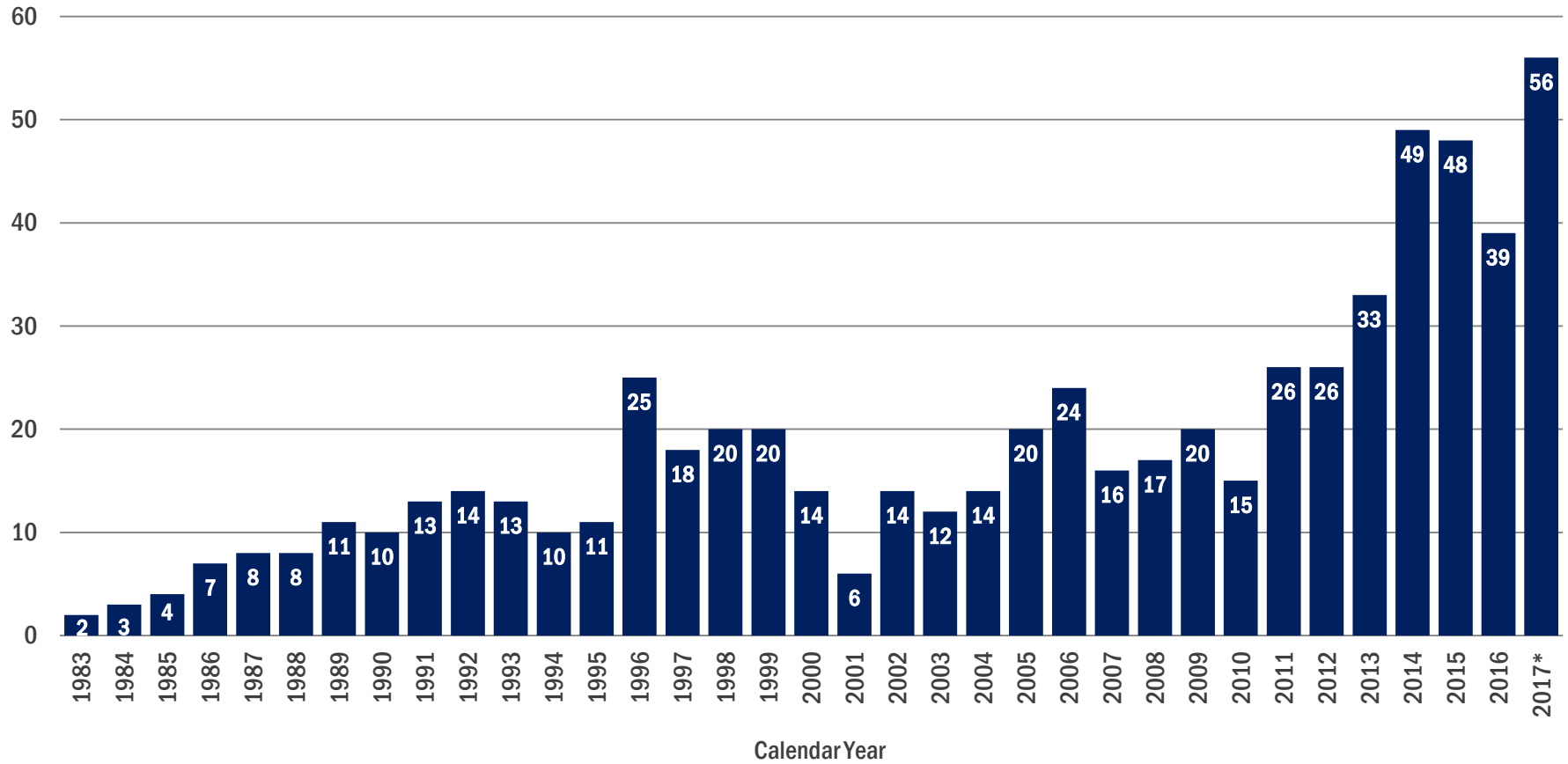


Data as of 11/30/2017

[†] 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. Percentages exclude pending applications from the denominator.



Approved Orphan Indications for all NDAs and BLAs[†] by CY

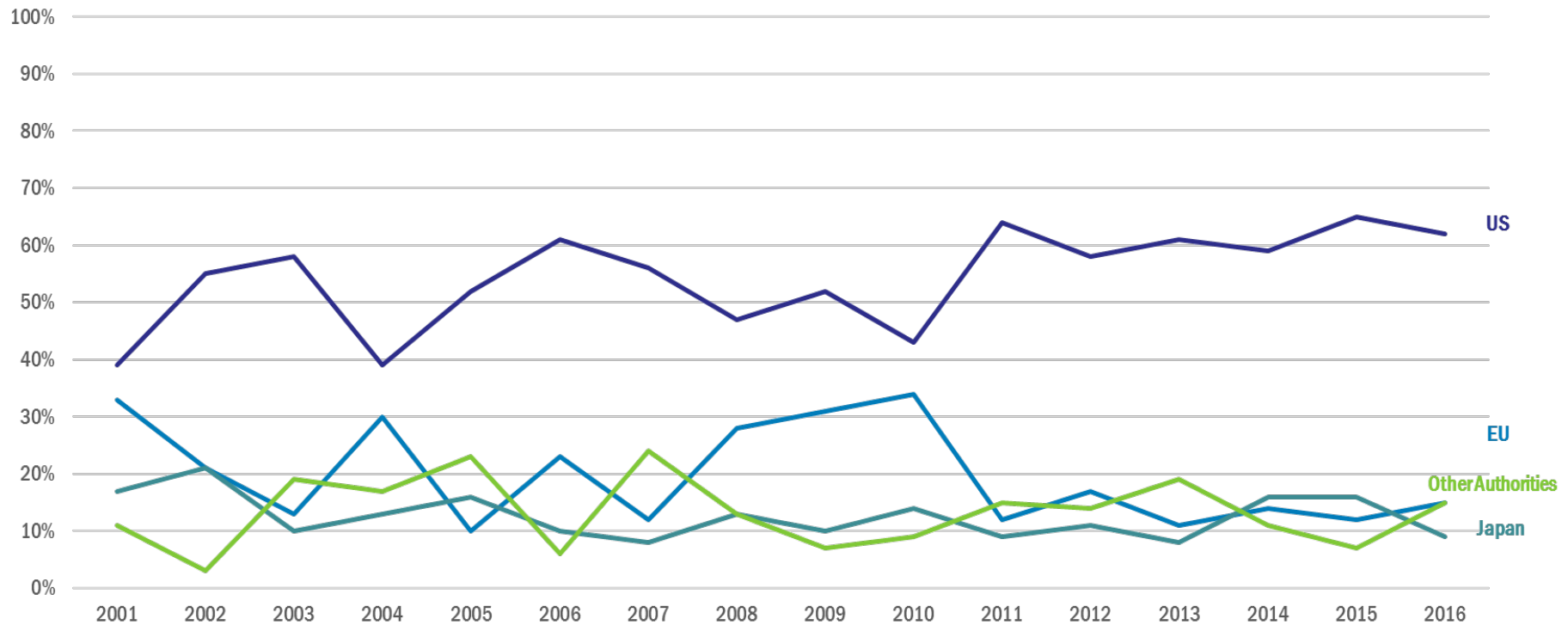


[†] Includes Efficacy Supplements

* Data as of 11/30/2017



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



Data as of 11/30/2017

Source: Scrip Magazine (1982 - 2006), Pharmaprojects/Citeline Pharma R&D Annual Review (2007 - 2016)



Snapshot of CY 2017

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 |
|------------|----------------------|-------------------------|----------------|----------------------------|----------------------|-------------------|-------------|----------------------|-------------|--------|
| TRULANCE | Green | Red | | Dark Blue | | | | | | |
| PARSABIV | Green | | | | | | | | | |
| EMFLAZA | Green | Red | Light Blue | | | Orange | Light Green | | Yellow | |
| SILIQ | Green | | | | | | | | | |
| XERMELO | Green | Red | | | | | | | Yellow | |
| KISQALI | Green | Red | | | | | | | | |
| XADAGO | Green | | | | | | | | | |
| SYMPROIC | Green | Red | | | | | | | | |
| BAVENCIO | Green | Red | | | | | | | Yellow | |
| ZEJULA | Green | Red | | | | | | | Yellow | |
| OCREVUS | Green | Red | | | | | | | | |
| DUPIXENT | Green | Red | | | | | | | | Yellow |
| AUSTEDO | Green | | | | | | | | | |
| INGREZZA | Green | Red | | Dark Blue | Blue | Orange | Light Green | | | |
| BRINEURA | Green | Red | Light Blue | Dark Blue | Blue | Orange | | | Yellow | |
| RYDAPT** | Green | Red | Light Blue | Dark Blue | Blue | Orange | Light Green | | Yellow | |
| TYMLOS | Green | Red | | Dark Blue | | | | | | |
| ALUNBRIG | Green | Red | | Dark Blue | Blue | Orange | | Orange | Yellow | |
| IMFINZI | Green | Red | | Dark Blue | Blue | Orange | | Orange | | |

✓ 70% of CY 2017 NME NDA/BLA approvals (28/40) designated and reviewed under priority review
 ✓ 17 breakthrough therapies approved, highest annual approval count to date for program
 ✓ 18 fast track designated products approved, also highest number approved in a given year

Data as of 11/30/2017

[†] 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 application is acted on within its first cycle due date.

** RYDAPT was submitted with two indications, of which one of the indications was granted Breakthrough Therapy designation and the other granted Fast Track designation.

QIDP - Qualified Infectious Disease Product



Snapshot of CY 2017

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 |
|--------------|----------------------|-------------------------|----------------|----------------------------|----------------------|-------------------|-------------|----------------------|-------------|-----------|
| RADICAVA | Green | Red | Blue | | | | | | Yellow | |
| KEVZARA | Green | | | | | | | | | |
| BAXDELA | Green | Red | | Dark Blue | | Orange | Light Green | | | Dark Blue |
| BEVYXXA | Green | Red | | Dark Blue | | Orange | Light Green | | | |
| TREMFYA | Green | Red | | Dark Blue | | Orange | | | | |
| NERLYNX | Green | | | | | | | | | |
| VOSEVI | Green | | | | | | | | | |
| IDHIFA | Green | | | | | | | | Yellow | |
| MAVYRET | Green | | | | | | | | | |
| BESPONSA | Green | | | | | | | | Yellow | |
| BENZNIDAZOLE | Green | | | | | | | | | |
| VABOMERE | Green | | | | | | | | | Dark Blue |
| ALIQOPA | Green | | | | | | | | Yellow | |
| SOLOSEC | Green | Red | | | | Orange | Light Green | | | Dark Blue |
| VERZENIO | Green | Red | | Dark Blue | Blue | Orange | Light Green | | | |
| CALQUENCE | Green | Red | | Dark Blue | Blue | Orange | | Orange | Yellow | |
| VYZULTA | Green | | | | | | | | | |
| PREVMIS | Green | Red | Blue | Dark Blue | Blue | Orange | Light Green | | Yellow | |
| FAENRA | Green | Red | | Dark Blue | | | | | | |
| MEPSEVI | Green | Red | Blue | Dark Blue | | Orange | Light Green | | Yellow | |
| HEMLIBRA | Green | Red | Blue | Dark Blue | Blue | Orange | | | Yellow | |

Over 2/3 of 2017 NME NDA/BLA approvals used more than one expedited development or review program

Data as of 11/30/2017

[†] 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 application is acted on within its first cycle due date.

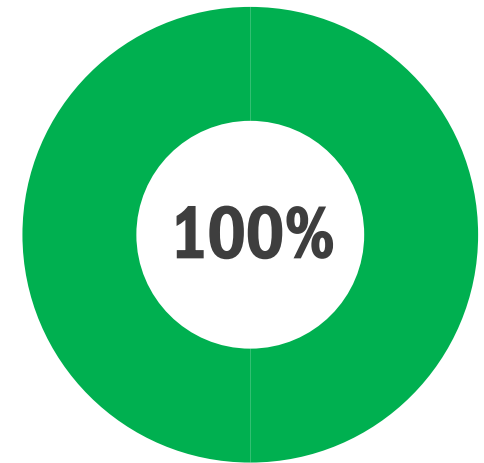
QIDP - Qualified Infectious Disease Product



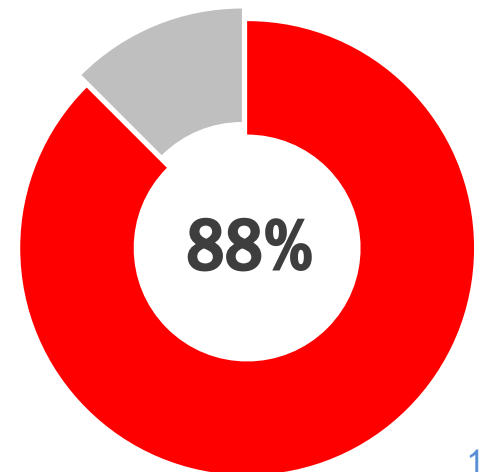
In CY 2017, CDER Continued To Ensure The Efficiency Of First Cycle Review

- All of the (100%) NMEs/BLAs approved to date in 2017 met their PDUFA goal dates
- Almost nine out of 10 (88%) of the drugs approved to date in 2017 were approved in the first review cycle

Met PDUFA Goal Date



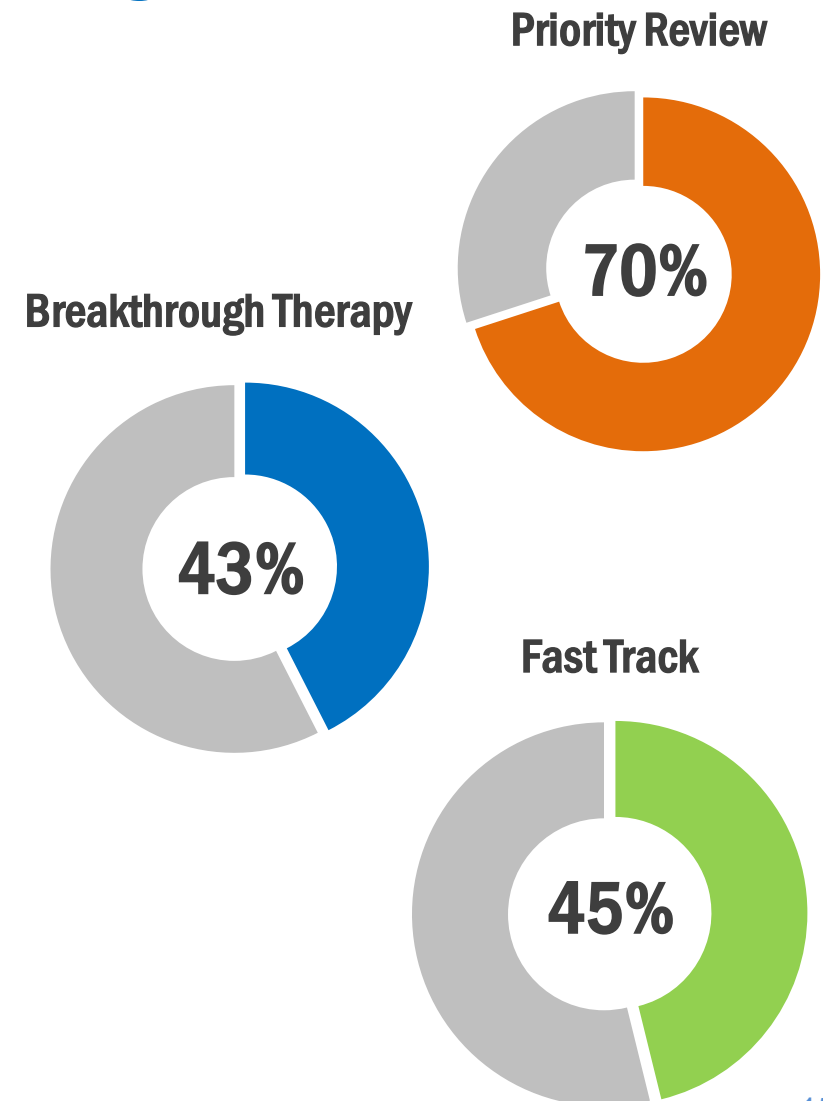
Approved on First Cycle





Utilization of Expedited Development and Review Programs Remained High in 2017

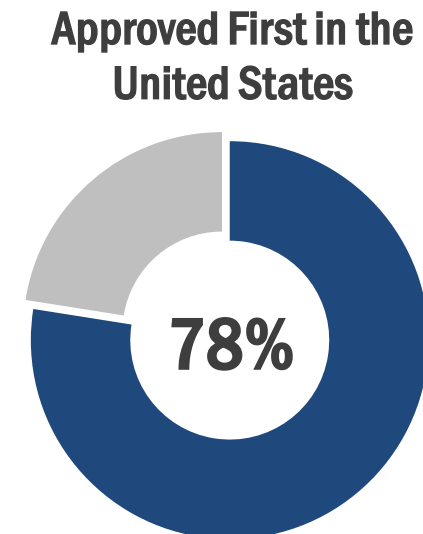
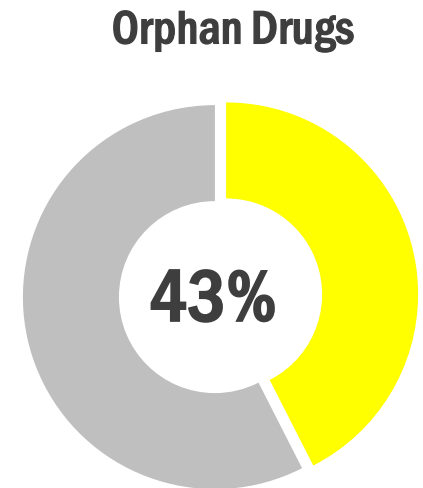
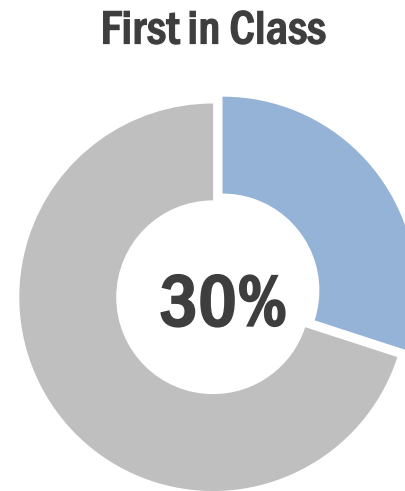
- More than two – thirds (70%) of the drugs approved to date in 2017 were approved under Priority Review
- About four out of ten (43%) of the drugs approved to date in 2017 received Breakthrough Therapy designation
- Almost half (45%) of the drugs approved to date in 2017 received Fast Track designation





2017 Continues A Strong Track Record For Drug Innovation

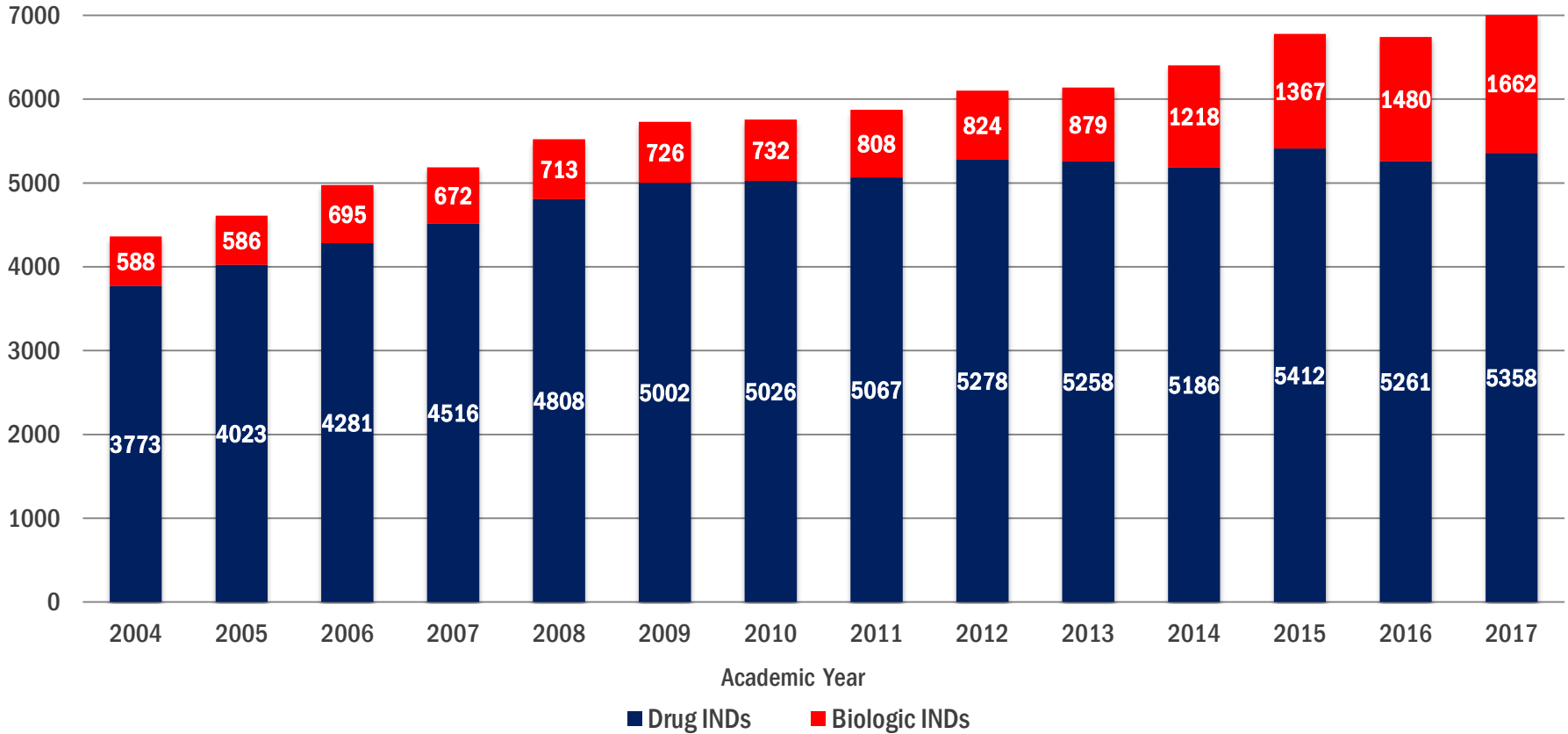
- About four out of ten (43%) of the drugs approved to date in 2017 are orphan drugs
- Almost a third (30%) of the drugs approved to date in 2017 are the first in their class
- Over three – quarters (78%) of the drugs approved to date in 2017 were first approved in the U.S.





Development Phase Work Continued to Grow in 2017

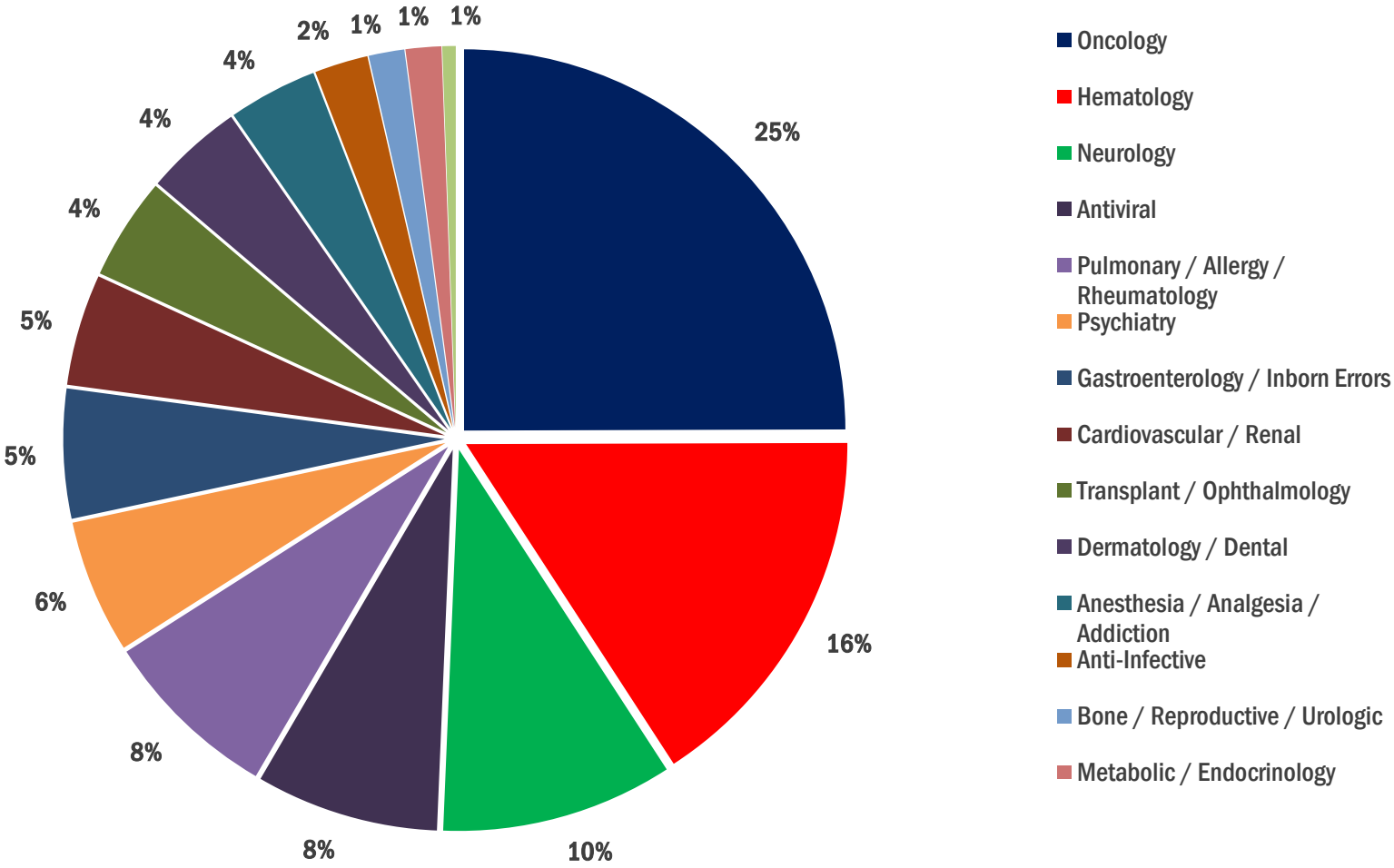
Commercial INDs With Activity



Data are from the PDUFA Workload Adjuster and represent a 12 month period of July 1st - June 30th



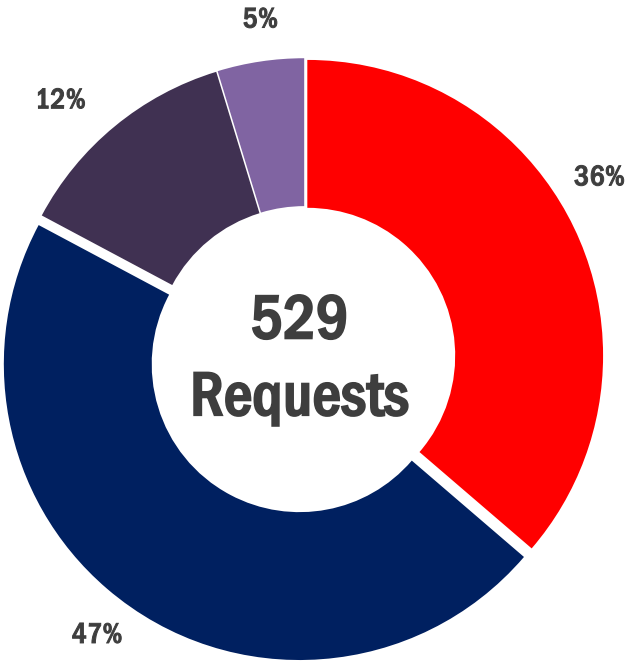
CDER Breakthrough Therapy Requests by Division



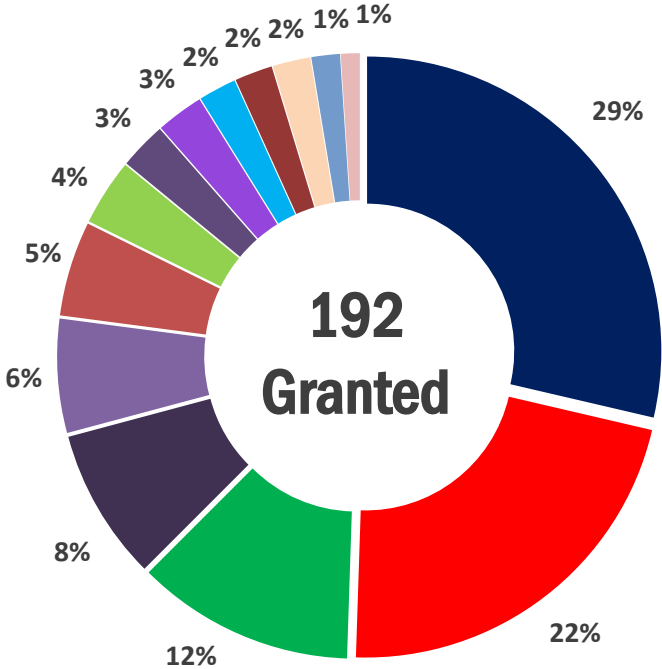
Data as of 11/30/2017



CDER Has Granted 192 Breakthrough Therapy Designations Since Inception



■ Granted ■ Denied ■ Withdrawn ■ Pending

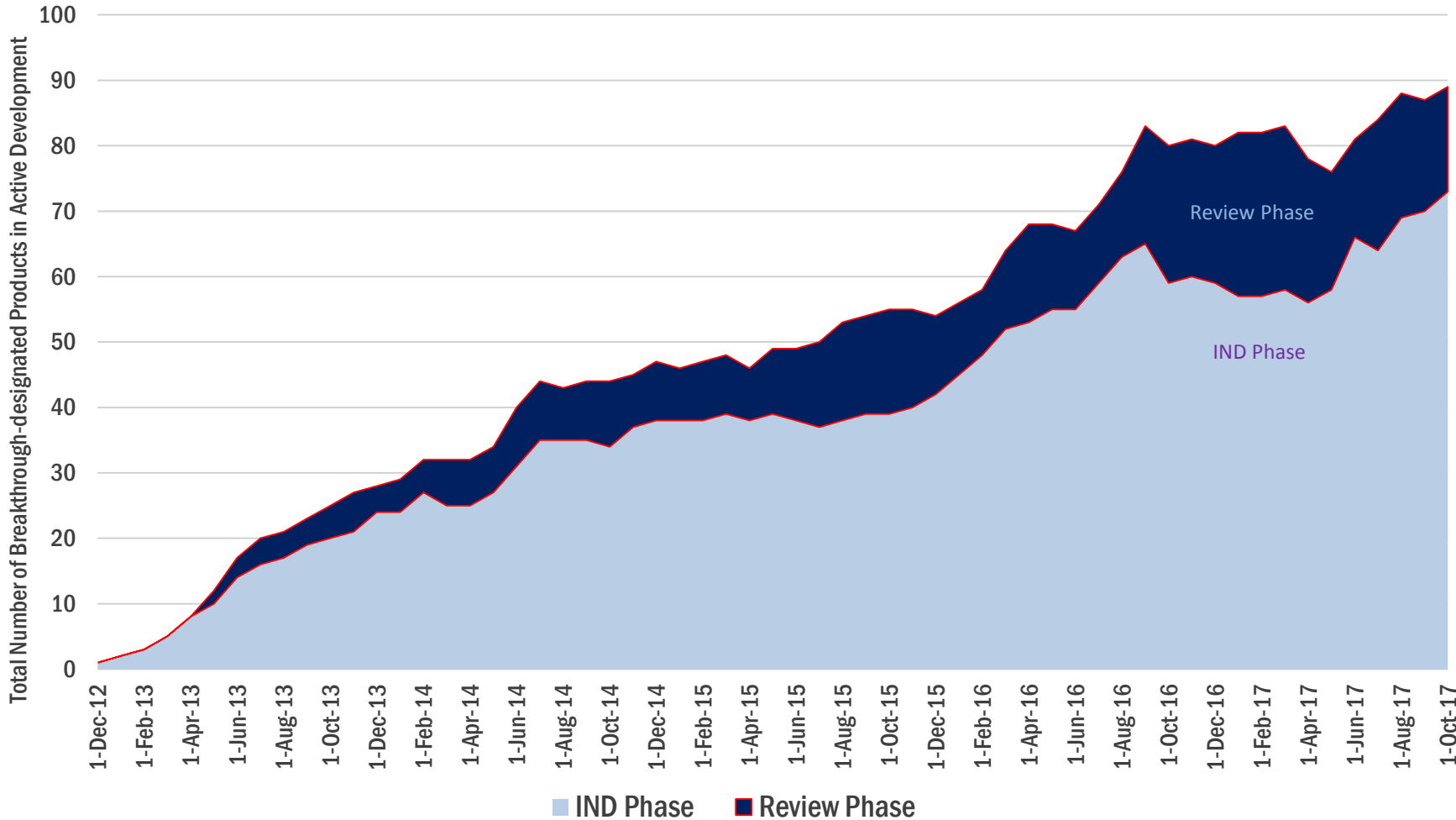


- Oncology
- Hematology
- Antiviral
- Pulmonary / Allergy / Rheumatology
- Psychiatry
- Gastroenterology / Inborn Errors
- Dermatology / Dental
- Anti-Infective
- Neurology
- Anesthesia / Analgesia / Addiction
- Transplant / Ophthalmology
- Cardiovascular / Renal
- Metabolic / Endocrinology
- Bone / Reproductive / Urologic

Data as of 11/30/2017



CDER Number of Breakthrough-Designated Development Programs Continues to Grow

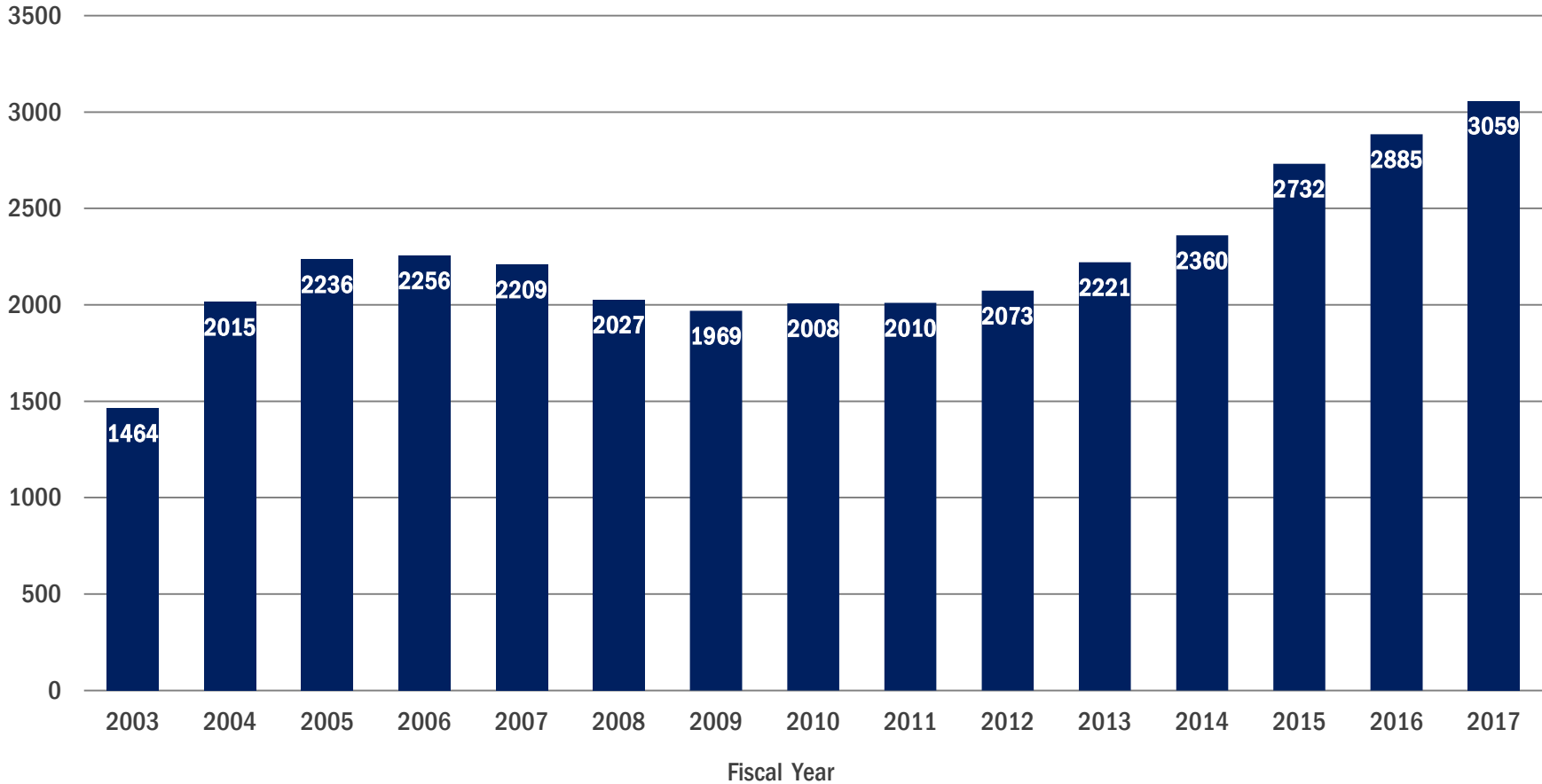


* Data as of 11/30/17. Figures includes total # of granted breakthrough designations for drug/indications under active IND development but have not yet received marketing approval or rescission decision.



CDER PDUFA

Formal Meeting Requests by FY



Data as of 9/30/2017

BLAs were transferred to CDER in FY2004



Meeting Management Changes in PDUFA VI

- End-of-Phase 2* meetings are now in a new category, Type B (EOP) meetings with unique parameters
 - Earlier notification that meeting is granted
 - Earlier submission of background package
 - FDA commits to send preliminary comments
 - Industry commits to respond to prelim comments
 - 70-day scheduling goal
- Type C meetings also changed
 - Earlier submission of background package
 - FDA commits to send preliminary comments
 - Industry commits to respond to prelim comments
- Written Response Only meetings: Sponsors may request this option for any meeting category

* Certain EOP1 meetings (e.g., 21 CFR Part 312 Subpart E or 21 CFR Part 314 Subpart H) are also included in this category



New Meeting in PDUFA VI: Early Consultations on New Surrogate Endpoints

- Early consultation can be important when a sponsor intends to use a biomarker as a new surrogate endpoint
- Consultation is intended to discuss feasibility of the surrogate as a primary endpoint, any knowledge gaps, and how these gaps should be addressed
- Consultations will be a Type C meeting with the following modifications:
 - Meeting background package is due at time of request and must include preliminary human data indicating the impact of drug on biomarker
 - Meeting preparation will involve CDER's Medical Policy Council
 - Meetings will be F2F; they will not be converted to a Written Response Only meeting

Looking ahead to 2018

- Ensure that recruitment and hiring of new drugs program staff continues to be a priority
 - 1108 FTEs on-board January 1, 2017
 - 1198 FTEs projected to be on-board by December 31, 2017
 - *Net* addition of 90 FTEs in 2017
- Continued implementation of new PDUFA VI and BsUFA II agreements, other aspects of FDARA and 21st Century Cures
- Continued ongoing critical evaluation of new drug regulatory program operations to ensure that we can meet program demands *and* our public health obligations to the American people

