Prescription Drug User Fee Act (PDUFA) Overview and Reauthorization

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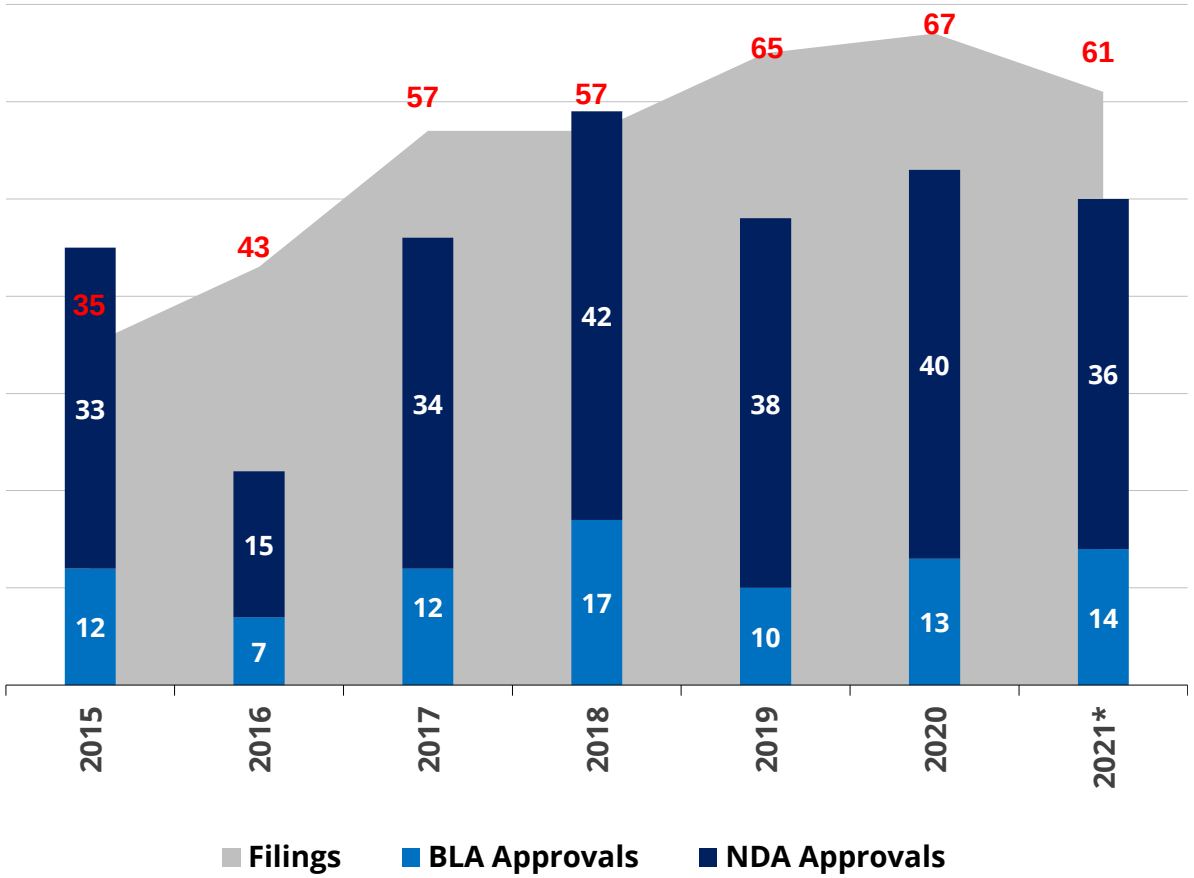
Agenda

- PDUFA Background
- PDUFA VII Proposed Enhancements
- Reauthorization Process

What is PDUFA? Why is it important?

Trends in PDUFA Workload – NME Filings and Approvals



323

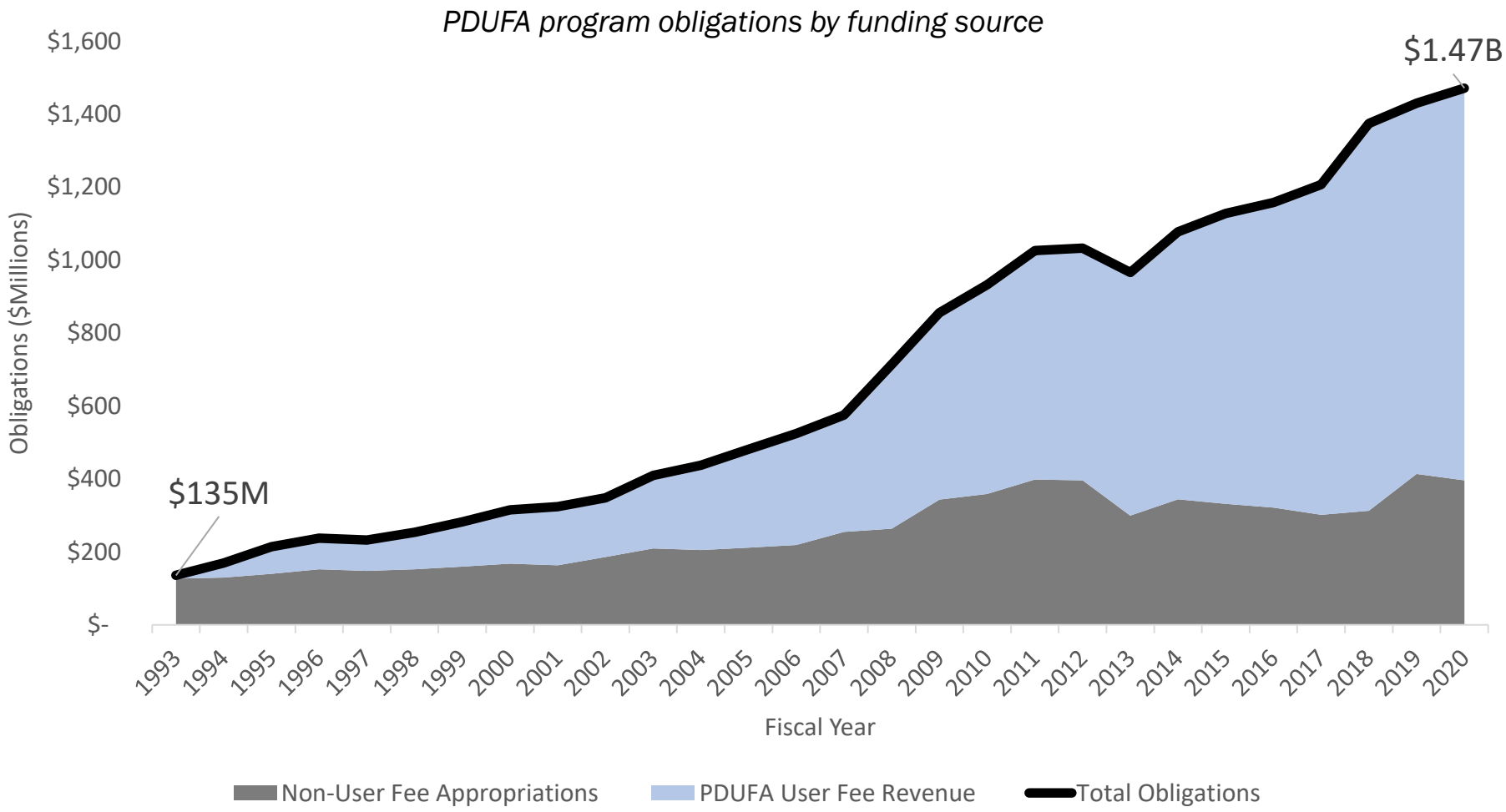
NME NDAs/BLAs Approved Since 2015

† 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 December 31st, 2021. 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.

User fee revenue is critical to the program



PDUFA user fee revenue funded **7%** of the program in FY1993 to **73%** in FY2020.

Basic User Fee Construct

- What the agreements are:
  - Commitments relate to specific aspects of activities in “process for the review of [medical products]”
  - Commitments and/or associated statutory changes also include mechanics of user-fee program (e.g., how fees are collected, fee types, products covered by each fee)
- What the agreements are not:
  - User fee commitment letters are not policy documents (e.g., FDA may commit to issuing guidance on a particular topic, but does not discuss or commit to what the substance of the policy would be)

PDUFA Performance commitments and fee funding have evolved since 1992

PDUFA | *1993-1997*
Added funds for pre-market review; reduced backlog and set predictable timelines (goals) for review action

PDUFA II (FDAMA) | *1998-2002*
Shortened review timelines, added review goals; added process and procedure goals; added some funding

PDUFA III (BT Preparedness & Response Act) | *2003-2007*
Significantly added funding; increased interaction in first review cycle (GRMPs); allowed limited support for post-market safety

PDUFA IV (FDAAA) | *2008-2012*
Increased and stabilized base funding; enhanced pre-market review; modernized post-market safety system

PDUFA V (FDASIA) | *2013-2017*
Small increase to base funding; review enhancements increased communication with sponsors; strengthened regulatory science & post-market safety; set electronic data standards

PDUFA VI (FDARA) | *2018-2022*
Modernized the user fee structure; focused on HR and financial management improvement; created capacity planning capability; enhanced use of regulatory tools via benefit-risk, patient-focused drug development, complex innovative trial designs, model informed drug development; enhanced staffing for breakthrough therapy reviews; focused on communication with industry; explored RWE in regulatory decision-making

PDUFA VI performance

- Performance enhancement goals (to-date)
  - 16 guidances
  - 39 public meetings and workshops
  - 70 implemented or updated programs/processes
  - 13 internal documents
  - 16 public reports
  - 2 implementation plan
  - 49 web, list, database updates
  - 1 hiring goal

- Met 86% of review goals (FY18-FY20)*
  - FY18 – 83%
  - FY19 – 92%
  - FY20 – 83%

Note: *This metric only contains CDER data and may not match the FDA Annual Performance Reports, which also include CBER data.

Overall Themes of FDA-Industry Discussions in PDUFA VII and Proposed Enhancements

- **CBER |** Enhancing CBER's capacity to guide development and review innovative products such as Cell and Gene Therapies
- **Pre-Market |** Introducing new approaches to improve efficiency and expand communication in the human drugs review program
- **Regulatory Decision Tools |** Continuing application of innovative methods and tools to enhance regulatory decision-making
- **Manufacturing |** Facilitating manufacturing readiness and use of innovative manufacturing technologies
- **Post-Market |** Ensuring safe use of medicines through continued enhancements to our drug safety system
- **Digital Health and Informatics |** Utilizing modern technology and supporting bioinformatics to enhance and streamline drug development and review
- **Finance |** Enhancing financial management and transparency
- **Hiring and Retention |** Focusing on the strategic hiring and retention of world-class technical and scientific staff

Pre-Market (1)

Split Real Time Application Review (STAR)

- A new pilot program (STAR) for certain efficacy supplements that seeks to expedite patient access to novel uses for existing therapies by supporting initiation of review earlier than would otherwise occur and therefore potentially allowing for earlier approval.
- Also includes a public-facing webpage, public workshop, and assessment.

PMRs/PMCs

- New process, timelines, and performance goals for pre-approval review of postmarketing requirements (PMRs) to ensure the timely availability of information on the safety and efficacy of therapies.
- A new process for sponsors to request review of existing PMRs.
- Both will include updating relevant MAPPs/SOPs/guidances.

Pre-Market (2)

Meeting Management: Best Practices, Type D Meetings and INTERACT

- Two new meeting types to expand communication and feedback during the drug development process. INitial Targeted Engagement for Regulatory Advice on CBER/CDER ProducTs (INTERACT) meeting is intended to facilitate IND-enabling efforts where a sponsor is facing a novel, challenging issue that might otherwise delay progress of the product towards entry into the clinic in the absence of this early FDA input. The new Type D meeting allows for quicker discussion on a narrow set of issues (no more than 2 focused topics) between FDA and a sponsor, such as a follow-up question that raises a new issue after a formal meeting.
- Introduces a new follow-up opportunity for sponsors to submit clarifying questions after meetings or a WRO to ensure sponsor's understanding of FDA feedback. This applies to all meeting types.
- Includes a public workshop, training, and updated guidance on best practices in meeting management and communication during between sponsors and FDA during drug development.

Rare Diseases Endpoint Advancement (RDEA) Pilot

- Building on the success of the rare disease programs in CDER and CBER, a new pilot program to advance rare disease drug development by providing a mechanism for sponsor discussions with FDA throughout the efficacy endpoint development process.
- Includes multiple public workshops.

Pre-Market (3)

Human Factors (HFs) and Use-Related Risk Analyses (URRAs) Reviews

- New procedures and timelines for use-related risk analysis and human factor validation study protocols to advance the development of drug-device and biologic-device combination products.
- Includes guidance on considerations related to combination products.

Real-World Evidence Pilot

- A pilot program that seeks to improve the quality and acceptability of real-world evidence (RWE) based approaches in support of new intended labeling claims, including approval of new indications of approved medical products or to satisfy post-approval study requirements.
- Includes annual reporting on pilot submissions, a public workshop or meeting, and updates to existing RWE-related guidances.

Regulatory Decision Tools

Advancing Patient's Voice in Drug Development and Decision-Making

- Expanded staff training and outreach to stakeholders with emphasis on Patient Focused Drug Development methods and tools-related guidance and practice; gathering public input and holding workshops on methodological issues and other issues of greatest interest.
- Continued work on developing a virtual catalog of standard core COAs seeking support of non-user fee funds.
- Issuing a guidance on use and submission of patient preference information.

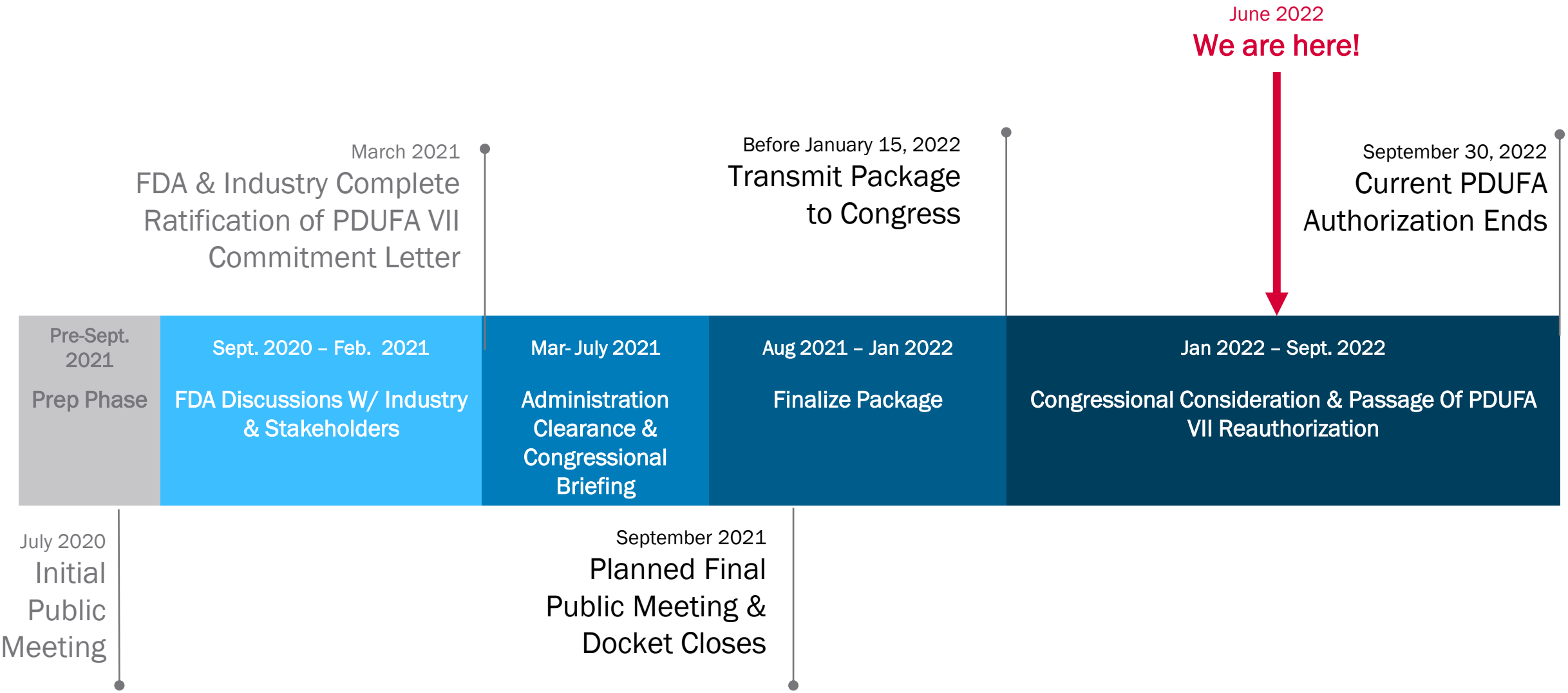
Continuation of Model-Informed Drug Development (MIDD)

- Advances the PDUFA VI pilot into a program to further advance and integrate the development and application of exposure-based, biological, and statistical models in drug development and regulatory review.

Continuation of Complex Innovative Trial Designs (CID)

- Advances the PDUFA VI pilot into a program with the goal to facilitate the advancement and use of complex adaptive, Bayesian, and other novel clinical trial designs.
- Includes a public workshop to discuss aspects of complex adaptive, Bayesian, and other novel trial designs, and guidance on use of Bayesian methodology in clinical trials.

PDUFA VII Reauthorization Timeline



Thank you