FRIENDS OF CANCER RESEARCH

Annual Meeting

Panel 3

Real-time Oncology Review: Streamlining Data Submissions and Ensuring Data Quality

#FriendsAM18

Wifi: RitzCarlton_CONFERENCE Password: fcr18

Panel 3 Participants

Moderator: Michael McCaughan, Prevision Policy

- Giuseppe Randazzo, U.S. FDA
- Jennifer Gao, U.S. FDA
- Jiten Rana, Novartis Pharmaceuticals
- Jonathan Cheng, Merck & Co., Inc.
- Karen Jones, Genentech, A Member of the Roche Group
- Katherine Couvillon, Patient Advocate

U.S. FOOD & DRUG ADMINISTRATION

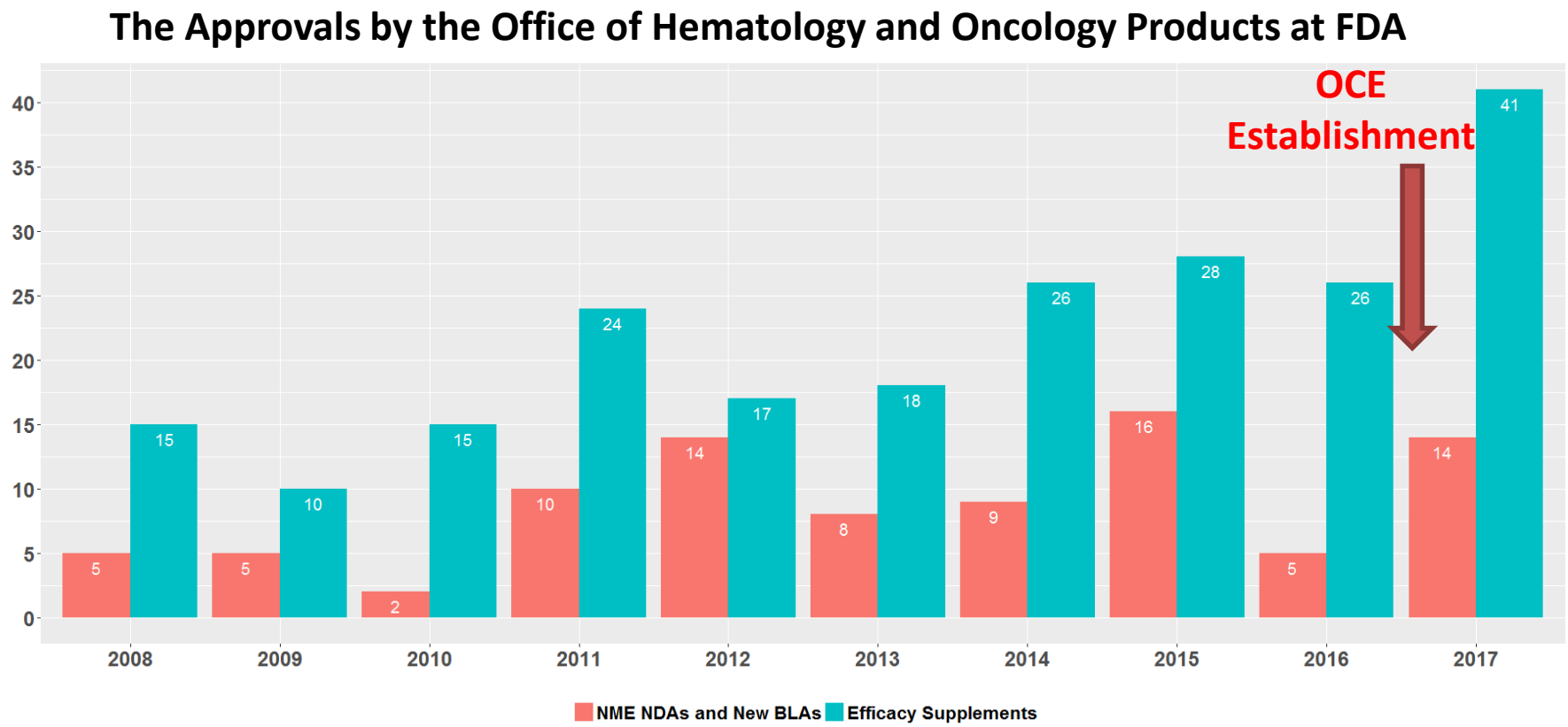
FDA Oncology Center of Excellence Pilot Programs: Real-Time Oncology Review (RTOR) & Assessment Aid (AAid)

Gideon Blumenthal, MD
Jinzhong Liu, PhD
Qi Liu, PhD
Richard Pazdur, MD

Friends of Cancer Research Annual Meeting

13-November-2018

Advances in Anticancer Drug Development Calls for Innovation to Improve Regulatory Efficiency



Oncology Center of Excellence (OCE) Mission Statement: **to achieve patient-centered regulatory decision-making through innovation and collaboration.**

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- **Office of Biostatistics**
  - Rajeshwari Sridhara
  - Thomas Gwise
  - Kun He
  - Lisa Rodriguez
  - Jonathon Vallejo
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  - Lola Luo
- **Office of Clinical Pharmacology**
  - Issam Zineh
  - Atiqur Rahman
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  - Michael Kopcha
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  - Steven Kozlowski
  - Don Henry
- **Office of Regulatory Affairs**
  - Alonza Cruse
  - Nancy Rolli
- **Industry Participants**
- **Patients and Patient Advocates**

Outline

1. Real-Time Oncology Review (RTOR)
2. Assessment Aid (AAid)
3. Pilot Cases
4. Feedback Received
5. Preliminary Conclusions

Real-Time Oncology Review (RTOR)

What Is It?

- A pilot review process allowing for earlier review of data prior to full application submission and interactive engagement with the applicant
- RTOR is currently implemented only for supplemental NDAs and BLAs
  - Inclusion Criteria
    - Drugs participating in an expedited program
    - Straight-forward study designs
    - Endpoints that can be easily interpreted
  - Exclusion Criteria:
    - Studies conducted exclusively outside the United States
    - Supplements with CMC formulation changes
    - Submissions with companion diagnostics
  - Flexibility may be exercised at the discretion of the review division

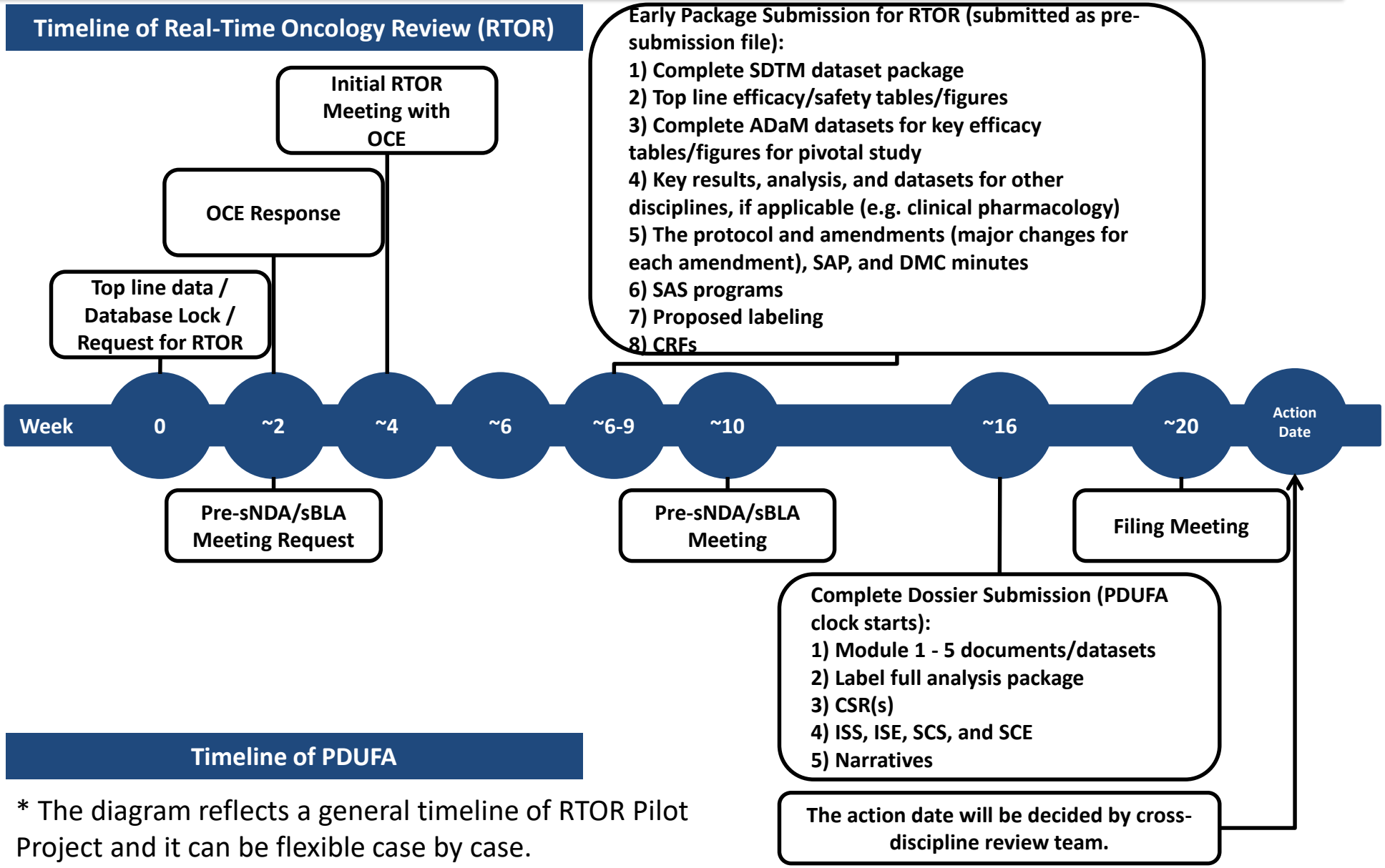
RTOR

Why Do We Use It?

- Problems
  - Lack of timely communication between the applicant and FDA can lead to issues in application submission
  - NDA/BLA submissions are not always “fit for purpose”
- Goals of RTOR
  1. Enable early interactive communication between applicants and FDA multi-disciplinary review teams
  2. Frontload some review activity and identify key regulatory issues prior to official application submission
  3. Explore a more effective review process while maintaining and improving review quality

RTOR

Proposed Timeline for sNDA/sBLA



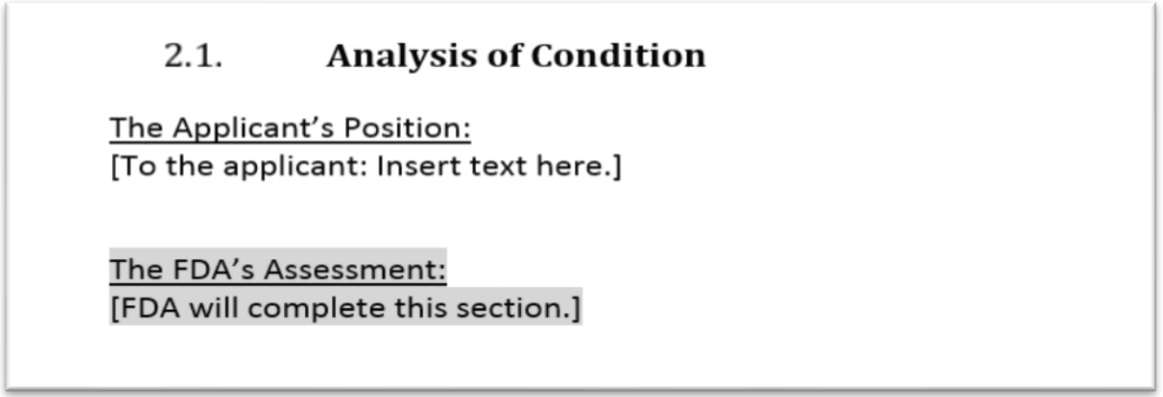
* The diagram reflects a general timeline of RTOR Pilot Project and it can be flexible case by case.

Assessment Aid (AAid)

What Is It?

- A voluntary submission from the applicant to facilitate FDA's assessment of the NDA/BLA application
- Developed based on the FDA Multidisciplinary Review Template
- For most issues, the sections are divided into 2 parts:
  1) The Applicant's Position
  2) The FDA's Assessment
     - ✓ Whether we agree with the applicant
     - ✓ What are our additional findings

  An example:



2.1. **Analysis of Condition**

The Applicant's Position:
[To the applicant: Insert text here.]

The FDA's Assessment:
[FDA will complete this section.]

- The AAid serves as the FDA review document once completed

AAid

Why Do We Use It?

- The FDA's review should focus on assessment (critical thinking), not on repeating the applicant's analyses and statements

- The separation of the Applicant's positions and FDA's assessment clarifies:
  - the ownership of each statement
  - agreement/disagreement between the Applicant and the FDA

AAid

When/How Do We Use It?

- The AAid can be used
  - for both NMEs and supplements
  - alone or together with RTOR
- The AAid template is sent to the applicant during IND stage
- The Applicant fills in their positions, and send back the document around the time of the NDA/BLA submission
- The FDA review team adds their assessment to the same document

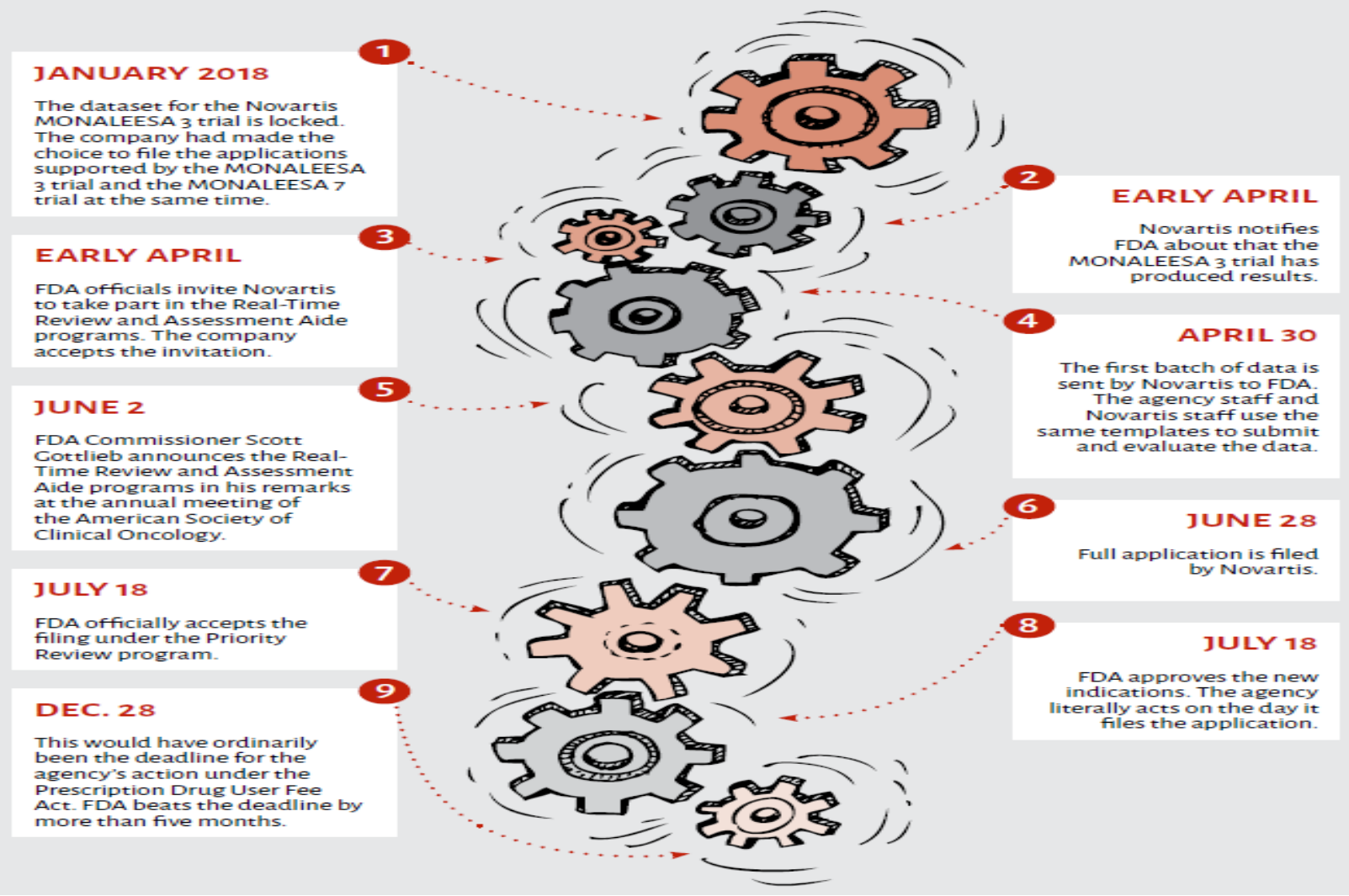
Pilot Cases

Completed RTOR and AAid Pilot Projects

Drug Name	FDA Review Division	sNDA/sBLA Submission Date	Approval Action (PDUFA date)	RTOR	AAid
Ribociclib	DOP1	6/28/2018	7/18/2018 (12/28/2018)	√	√
Pembrolizumab	DOP2	3/23/2018	8/20/2018 (9/23/2018)	√	
Carfilzomib	DHP	8/24/2018	9/28/2018 (2/24/2019)	√	√

Case Study

Ribociclib Review/Approval



* The Cancer Letter | July 20, 2018 | Vol 44 | Issue 29

Feedback Received

(from the FDA teams/the applicants who participated in the pilots)

- Survey has been conducted with the FDA review teams
- Post action feedback meetings were held with the applicants
- Identified key to success:
  - Early engagement between the FDA and the applicants
    - The applicants need to change the preparation order of the different parts of the submission
  - Clear communication
    - FDA internal communication
      - Expectations and timelines
    - Communication between the FDA and the applicants
      - What type of information is needed, and when

Preliminary Conclusions

- The RTOR and AAid pilot programs can be used to improve review efficiency, while maintaining or improving review quality
- The RTOR and AAid pilots helped expedite patient access to new treatment options
- Early engagement and clear communication are critical for the success of the programs

Further information at OCE website

- RTOR: https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/OCE/ucm612927.htm
- AAid: https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/OCE/ucm612923.htm

Thank You

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