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CDER Breakthrough Therapy Program: What Happens Post-Designation?

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FDA

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Outline

- Regulatory Background
- CDER Breakthrough Designations
- CDER Breakthrough Actions
- Resources

Breakthrough Therapy Designation: An Expedited Program

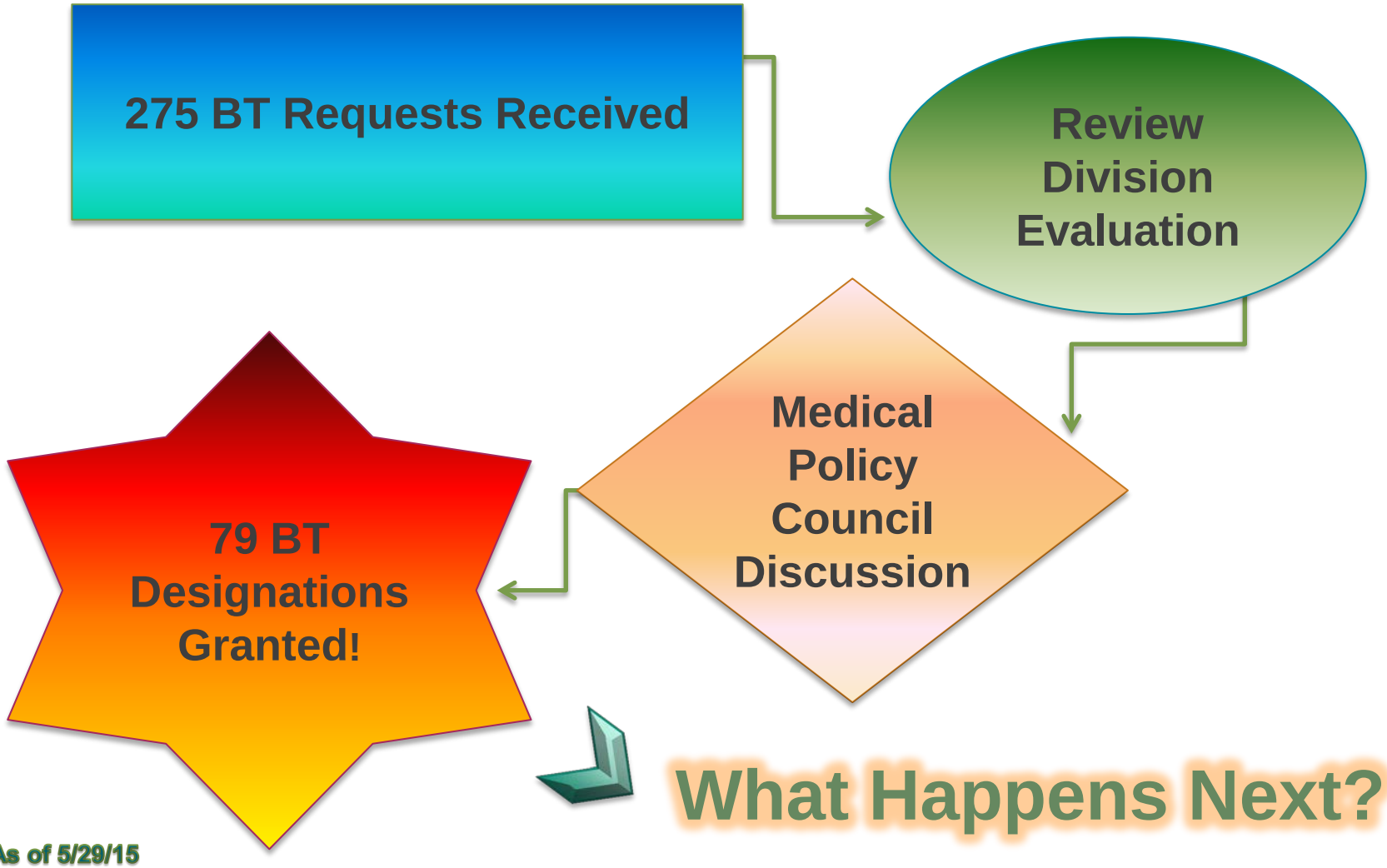
- For drugs that addresses an unmet medical need in the treatment of a serious or life-threatening condition
- Intended to help ensure that therapies for these conditions are approved & available to patients as soon as it can be concluded that the therapies' benefits justify their risks
- Allow for earlier attention to drugs that have promise in treating such conditions

FDASIA* 902 Provisions

- FDA will take actions to **expedite the development & review of the drug:**
  - Assign a cross-disciplinary project lead **(CDPL)**
  - **Hold meetings** with the sponsor throughout drug development
  - Provide timely **advice to & interactive communication** with the sponsor
  - Take steps to **ensure efficient clinical trial design**
  - **Involve senior managers** & experienced review staff

*Food and Drug Administration Safety and Innovation Act

CDER Breakthrough Therapy Designations*



*As of 5/29/15

CDPL Role

CDPL

Acts as a Scientific Liaison between all members of review team

Addresses & facilitates Issue resolution

Keeps management apprised of BT program status & progress

DIA DEVELOP INNOVATE ADVANCE

CDER-Sponsor Meetings

- Initial Comprehensive Multidisciplinary Breakthrough Meeting
  - Type B meeting to discuss the high-level plan for BTD drug development
- Subsequent Type B Meetings
  - Review team continues to meet w/sponsor throughout IND phase
- Critical Milestone Meetings
  - Likely to take place in at earlier time points in drug development

Breakthrough Therapies Considerations: Drug Development

Clinical

- **Trial design flexibility/innovative approaches**
- **Compressed drug development options**
- **Consideration for accelerated approval**

Product Quality

- **Expediting manufacturing development strategy**
- **Novel risk mitigation strategies**
- **Early facilities information**

Regulatory

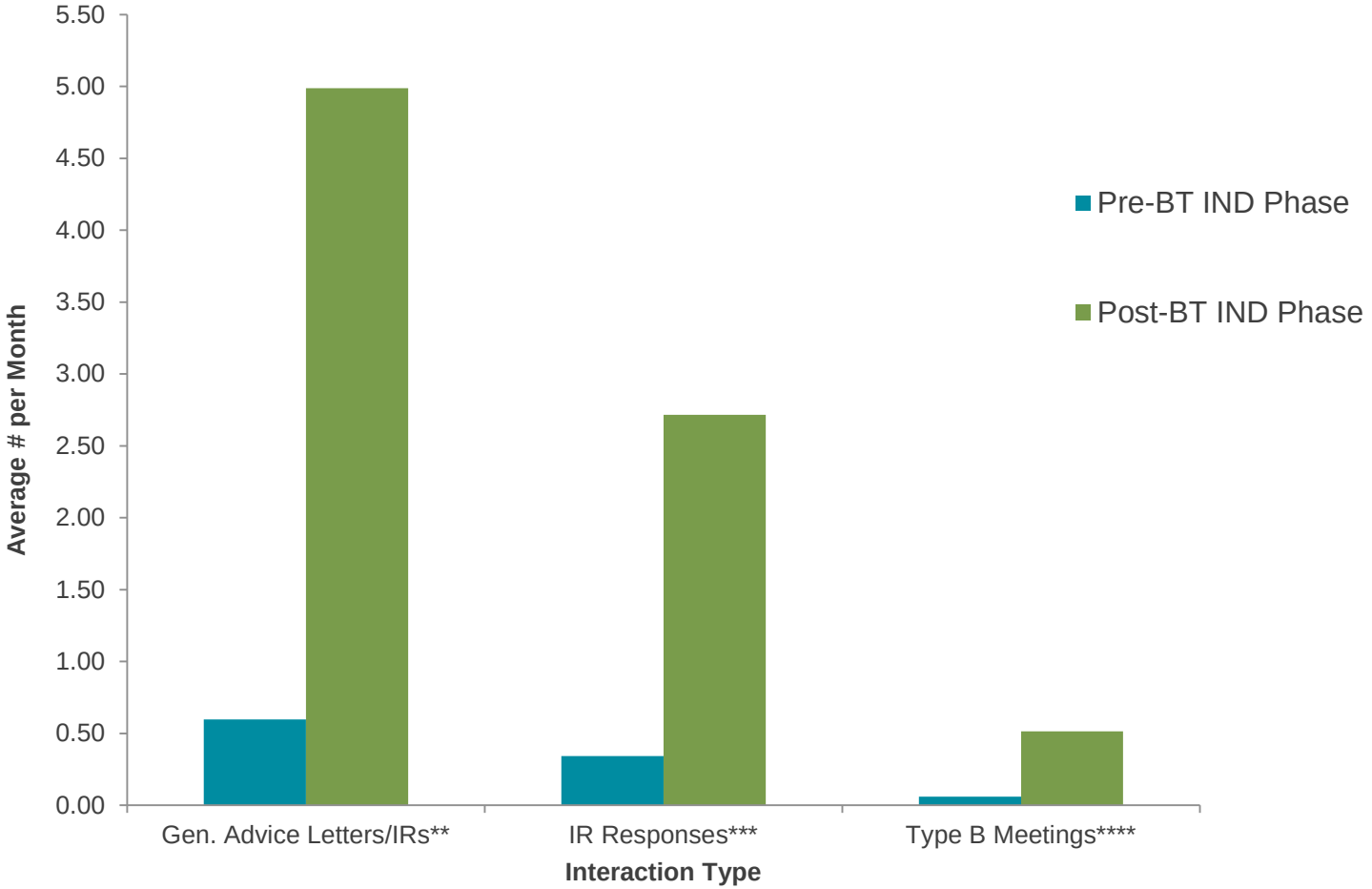
- **Proprietary name request plans**
- **Potential post-approval studies**
- **Expanded access plans**

CDER-Sponsor Communications Outside of Formal Meetings

- Telecons, information requests, & emails used as tools for focused discussions, rapid information exchange, & issue resolution
- Inquiries from sponsors
  - RPMs communicate anticipated timeline for a response, based on inquiry complexity
  - CDER responds within a few days; 30 days max

RPMs remain the point of contact!

CDER-Sponsor Communications: IND Phase



*Data reflect the 20 BT drugs that received BT designation during their IND phase and that submitted a marketing application by the end of FY2014. Note that CDER-sponsor interactions typically increase even for non-BT applications prior to the submission of a marketing application

**General Advice Letters and Information Requests issued by the FDA to the sponsor

***Sponsor responses to FDA Information Requests

****Type B meetings between the FDA and sponsor

CDER Review of BT Drug Development Programs

- Most submissions reviewed in 60 days or less*
  - Limited types of submissions require 90 days
- Review staff perform periodic high-level reviews of BTD drug development programs
  - Performed approximately every 3 to 6 months

*Per MAPP 6030.9: Good Review Practice: Good Review Management Principles and Practices for Effective IND Development and Review

Rescinding a BTD

- If BTD criteria are no longer met, CDER may rescind
- Intent to Rescind letter sent to sponsor
  - Sponsor has opportunity to provide additional data & rationale and/or request a meeting
- If determined BTD criteria continue to be met:
  - Plans for development of the drug discussed & communicated to sponsor
- If determined BTD criteria no longer met:
  - Designation is rescinded

Expedited Review - Marketing Applications

- CDER staff will consider an Expedited Review (ER) for each marketing application (MA) for BTD drugs
- ERs are:
  - A subset of priority reviews, and
  - Action is planned for at least one month prior to PDUFA goal date, if:
    - No unexpected review issues arise
    - Review team does not experience unexpected shift in work priorities or staffing

CDER-Sponsor Meetings & Interactions: Expedited Review

- Early dialog on timing of planned MA submission
- Intent to conduct ER discussed at MA pre-submission meeting
- “Program”-related meetings occur earlier in review cycle
- Frequent discussions and exchange of information
- Rapid issue identification & resolution

Breakthrough Therapies Considerations: Marketing Application Review

Inspections

- Early submission of clinical site data sets
- Early communications re: planning & conduct
- Activities scheduled early in review

Product Quality

- Stability data options
- Innovative steps to insure product readiness for marketing
- Flexibility on planned late amendments

- Expedited review
- Rolling review encouraged & submissions reviewed early
- Increased use of post-marketing commitments and requirements

Advisory Committee Meetings

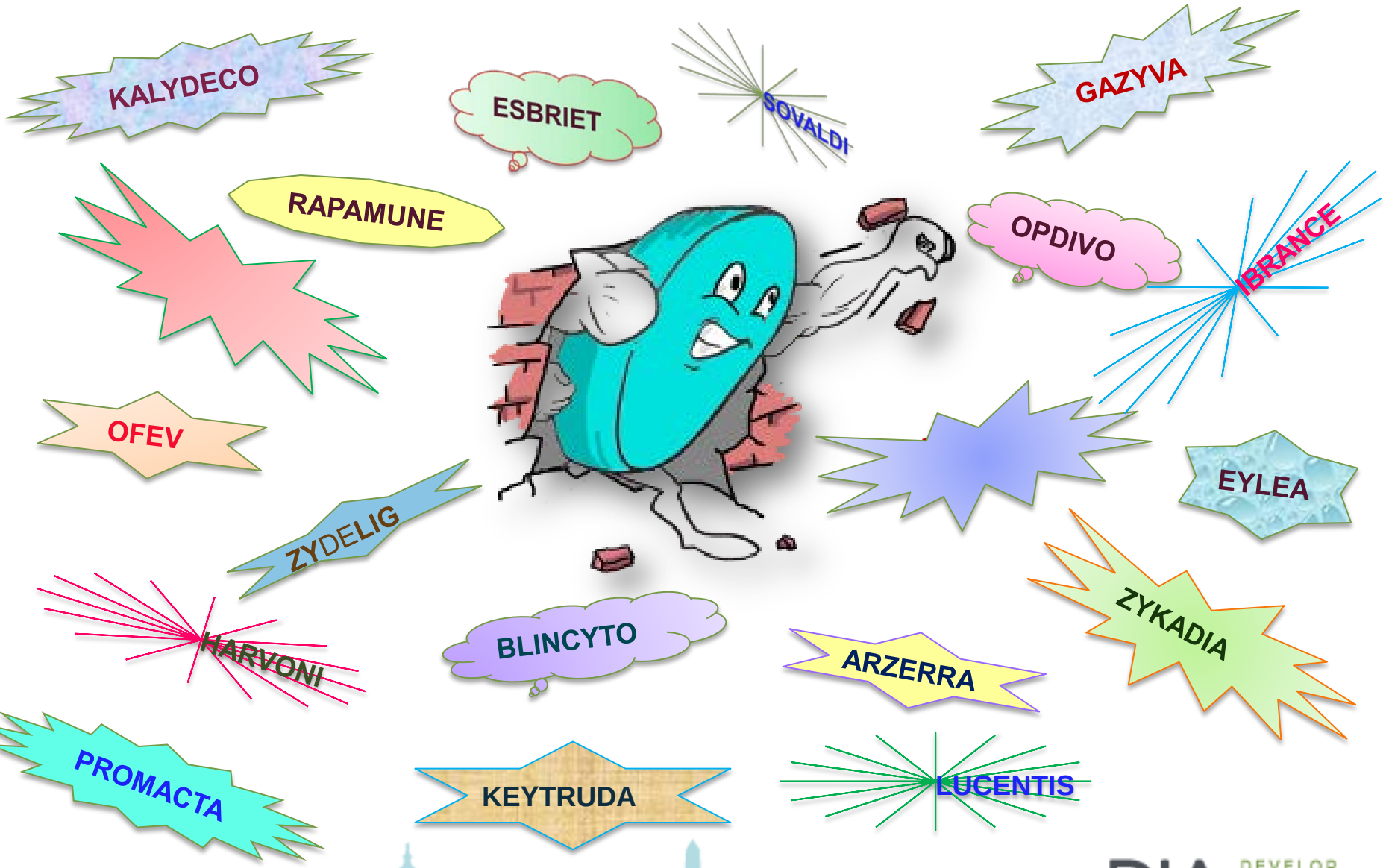
- AC meetings typically are not convened
  - BTD drugs generally have an acceptable:
    - Safety profile for indication
    - Clinical trial design & endpoints
  - Applications typically do not raise:
    - Unexpected efficacy issues
    - Significant public health questions
- Need for an AC evaluated on a case-by-base basis, and may be required

Senior Management Involvement

- Subordinate & Super-office* directors stay abreast of the status of BTD drugs and provide guidance through:
  - 1:1 meetings with CDPLs
  - Administrative rounds
  - Internal meetings with leadership teams
- Medical Policy Council**
  - BT Policy Meetings
  - Quarterly BTD Portfolio Reviews
  - BT Rescinding Meetings

*Super Office: An office that reports to the CDER Director and to which subordinate offices report. Subordinate Office: An office that reports to a super office.

BTD Approvals



BTD Program Resources

- MAPP 6025.6: Good Review Practice: Management of Breakthrough Therapy-Designated Drugs and Biologics

http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ManualofPoliciesProcedures/default.htm

- MAPP 6025.7: Good Review Practice: Review of Marketing Applications for Breakthrough Therapy-Designated Drugs and Biologics That Are Receiving an Expedited Review

http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ManualofPoliciesProcedures/UCM437281.pdf

- Guidance for Industry: Expedited Programs for Serious Conditions—Drugs and Biologics:

http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM358301.pdf

BTD Program Resources-2

- MAPP 6030.9: Good Review Practice: Good Review Management Principles and Practices for Effective IND Development and Review

http://www.fda.gov/downloads/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cder/manualofpoliciesprocedures/ucm349907.pdf

- BT Information on fda.gov:

http://www.fda.gov/regulatoryinformation/legislation/federalfooddrugandcosmeticactfdcact/significantamendmentstothefdcact/fdasia/ucm329491.htm

- Section 902 of FDASIA:

http://www.gpo.gov/fdsys/pkg/BILLS-112s3187enr/pdf/BILLS-112s3187enr.pdf

Thank You

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