Approved Products and Regulatory Considerations in Immune Thrombocytopenia

Roma Rajput, MD
Medical Officer
Division of Non-Malignant Hematology (DNH)
Office of Cardiology, Hematology, Endocrinology and Nephrology (OCHEN)
Food and Drug Administration (FDA)
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Department of Health and Human Services
Food and Drug Administration

Current as of:
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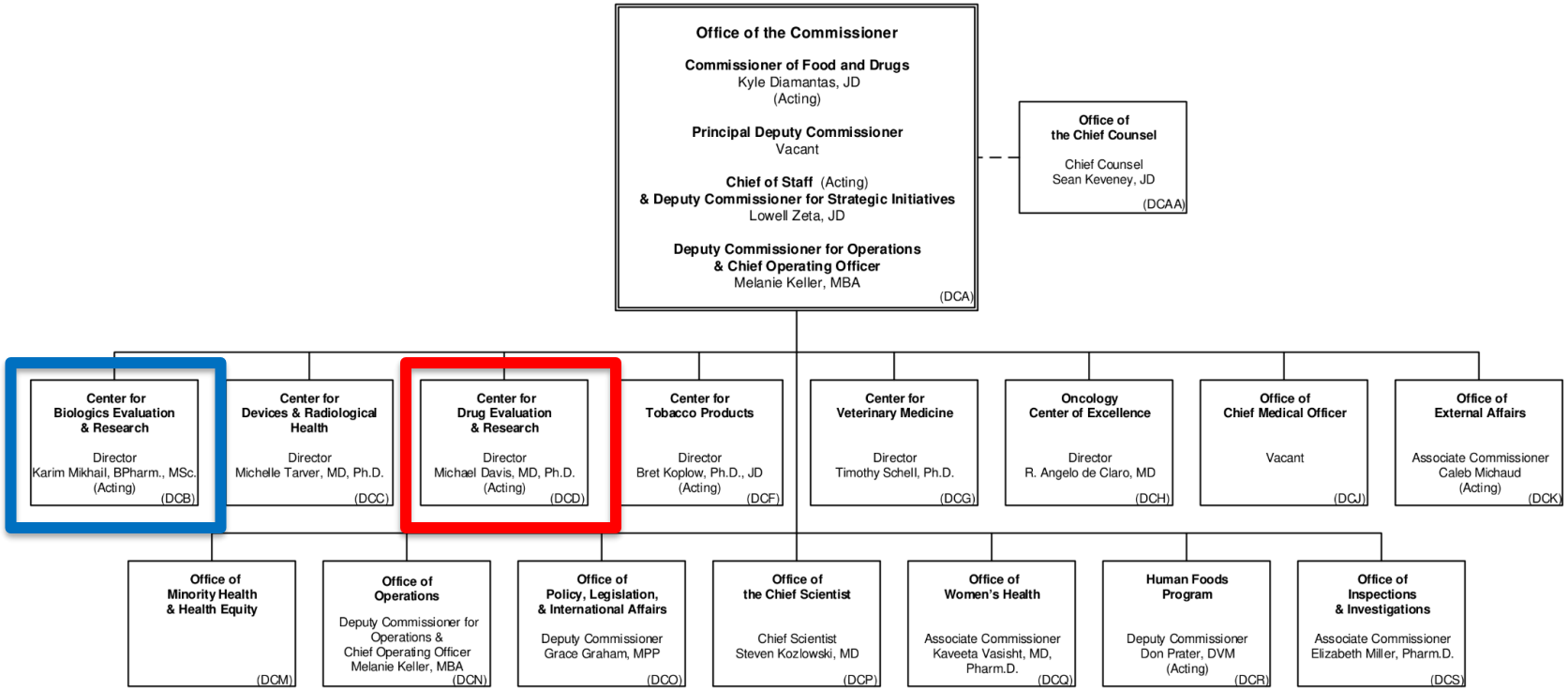

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Outline

- Substantial Evidence of Effectiveness for Drug Approval
- Challenges in rare disease drug development (ITP perspective)
- Overview of FDA CDER approved products in ITP

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FDA's Mission

- Includes protecting and promoting the public health by ensuring the **safety and efficacy** of drugs, biological products, and medical devices.
  - Examples of how this is done include:
    - Engagement with patients, family members, advocacy groups, clinicians; scientific, academic, and biotech/pharmaceutical companies

Source: What We Do | FDA

www.fda.gov

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Substantial Evidence of Effectiveness

- Demonstration of substantial evidence of effectiveness (SEE) is necessary for drug approval.
- Approaches to meeting SEE standard
  - **One adequate and well-controlled trial (AWC) plus confirmatory evidence**
  - Examples of types of data that could be considered confirmatory evidence
    - Clinical evidence from a related indication
    - Mechanistic or pharmacodynamic evidence
    - Evidence from a relevant animal model
    - Evidence from other members of the same pharmacological class
    - Natural history evidence
    - Real-world data or evidence
    - Evidence from expanded access use of an investigational drug

Source: Guidance for Industry: Demonstrating Substantial Evidence of Effectiveness for Human Drug and Biological Products (June 2026)
Source: Guidance for Industry: Demonstrating Substantial Evidence of Effectiveness With One Adequate and Well-Controlled Clinical Investigation and Confirmatory Evidence (September 2023)

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Substantial Evidence of Effectiveness (continued)

- **More than one adequate and well-controlled clinical investigation may be appropriate**
  - Needs of the Sponsor's specific development programs
  - Trial not sufficiently representative of broad population expected to use the drug
  - Trial insufficient to support a reliable safety and benefit-risk assessment
- Regulatory flexibility may be warranted in certain clinical circumstances

Source: Guidance for Industry: Demonstrating Substantial Evidence of Effectiveness for Human Drug and Biological Products (June 2026)
Source: Guidance for Industry: Demonstrating Substantial Evidence of Effectiveness With One Adequate and Well-Controlled Clinical Investigation and Confirmatory Evidence (September 2023)

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Some Challenges in Rare Disease Drug Development

- Natural history is often poorly understood.
- Diseases are progressive, serious, life-limiting and often lack adequate approved therapies – urgent needs, many have pediatric onset.
- Phenotypic and genotypic diversity within a disorder.
- Development programs often lack solid translational background.
- Drug development tools - outcome measures and biomarkers often lacking.
- Lack of precedent, including clinically meaningful endpoints, for drug development in many rare diseases.

Source: Janet Maynard, MD, Director of the Office of Rare Diseases, Pediatrics, Urologic and Reproductive Medicine (ORPURM)

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Orphan Drug Designation

- Orphan refers to products designated for rare diseases or conditions, stemming from the **Orphan Drug Act of 1983**.
- The drug must be intended to treat a rare disease or condition affecting fewer than **200,000** people in the United States.
- Benefits of Orphan Designation
  - **Market exclusivity** - Seven years of marketing exclusivity upon FDA approval
  - **Tax credits** – To defray the cost of conducting clinical trials
  - **Fee waivers** - Exemption from FDA user fees

Source: Guidance for Industry: Clarification of Orphan Designation of Drugs and Biologics for Pediatric Subpopulations of Common Diseases

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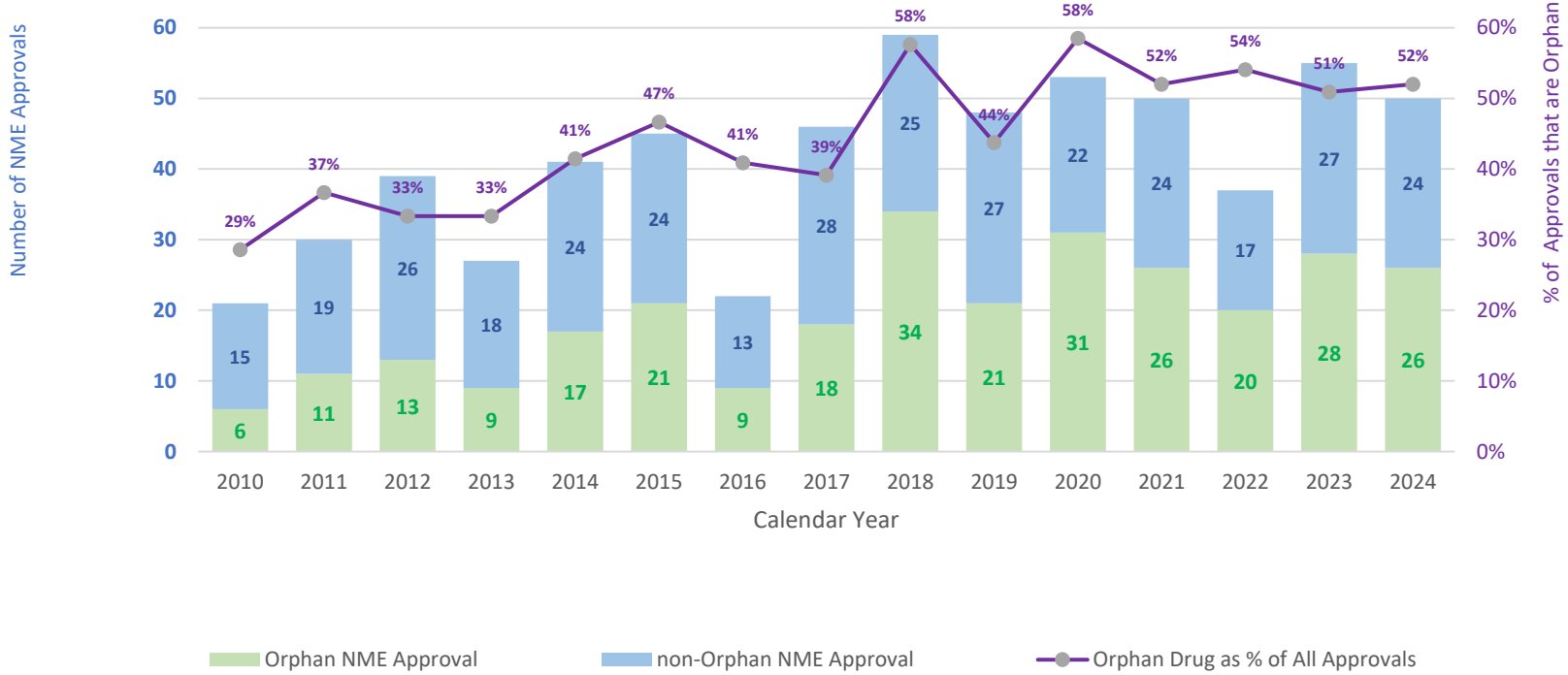
Proportion of CDER Novel Drug Approvals that are Orphan



Source: Janet Maynard, MD, Director of ORPURM

The Patient Voice at FDA
Patient Focused Drug Development (PFDD)

- **What is PFDD?**
  - FDA initiative that systematically gathers patient perspectives on their condition and available therapies
  - Mandated by 21st Century Cures Act requiring Agency to consider which outcomes matter most to patients and how they weigh benefits/risks of treatment
- **How PFDD Helps the FDA**
  - Patient input directly informs FDA benefit-risk assessments, helps identify unmet medical needs, and guides clinical trial design

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FDA CDER Approved Drugs for ITP

- **Nplate® (romiplostim)**
  - Approved 2008 for adult patients with ITP who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy
  - Approved 2018 for pediatric patients 1 year of age and older with ITP for at least 6 months who have had an insufficient response to corticosteroids, immunoglobulin, or splenectomy
- **Promacta® (eltrombopag)**
  - Approved 2008 for the treatment of thrombocytopenia in adult patients with chronic ITP who have had an insufficient response to corticosteroids, immunoglobulin, or splenectomy
  - Approved 2015 for pediatric patients one year and older with chronic ITP who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy
- **Tavalisse® (fostamatinib)**
  - Approved 2018 for treatment of thrombocytopenia in adult patients with chronic ITP who have had an insufficient response to a previous treatment
- **Doptelet ® (avatrombopag)**
  - Approved 2019 for thrombocytopenia in adult patients with chronic ITP who have had an insufficient response to a previous treatment
  - Approved 2025 for thrombocytopenia in pediatric patients one year and older with chronic ITP who have had an insufficient response to a previous treatment
- **Wayrilz® (rilzabrutinib)**
  - Approved 2025 for adult patients with persistent or chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment

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Endpoints for FDA CDER Approved ITP Products

- **Nplate® (romiplostim)**
  - Durable platelet response: Platelet count $\geq 50 \times 10^9$/L for at least 6 of the last 8 weeks of the 24-week treatment period in the absence of rescue medication at any time
- **Promacta® (eltrombopag)**
  - Platelet response: shift from a baseline platelet count $\leq 30 \times 10^9$/L to $\geq 50 \times 10^9$/L at any time during the treatment
  - Sustained platelet response: platelet count $\geq 50 \times 10^9$/L and $\leq 400 \times 10^9$/L for 6 out of the last 8 weeks of the 26-week treatment period in the absence of rescue medication at any time
- **Tavalisse® (fostamatinib)**
  - Stable platelet response: platelet count of at least 50×10^9/L on at least 4 of the 6 visits between Weeks 14 and 24
- **Doptelet ® (avatrombopag)**
  - Durable platelet response: proportion of patients achieving at least 6 out of 8 weekly platelet counts $\geq 50 \times 10^9$/L during the last 8 weeks of the 12-week treatment period in the absence of rescue medication
- **Wayrilz® (rilzabrutinib)**
  - Durable platelet response: weekly platelet count $\geq 50 \times 10^9$/L for ≥ two-thirds of at least 8 non-missing weekly scheduled platelet measurements during the last 12 weeks of the 24-week blinded treatment period in the absence of rescue therapy, provided that at least 2 non-missing weekly scheduled platelet measurements were $\geq 50 \times 10^9$/L during the last 6 weeks of the blinded treatment period

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