Orphan Products and Drug Development 2015

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What are Orphan's?

- Drug Development
- Rare Diseases
- Orphan Drug Act of 1983
- Rare Diseases Legislation Around the World
- Challenges
- Opportunities
- What the future holds

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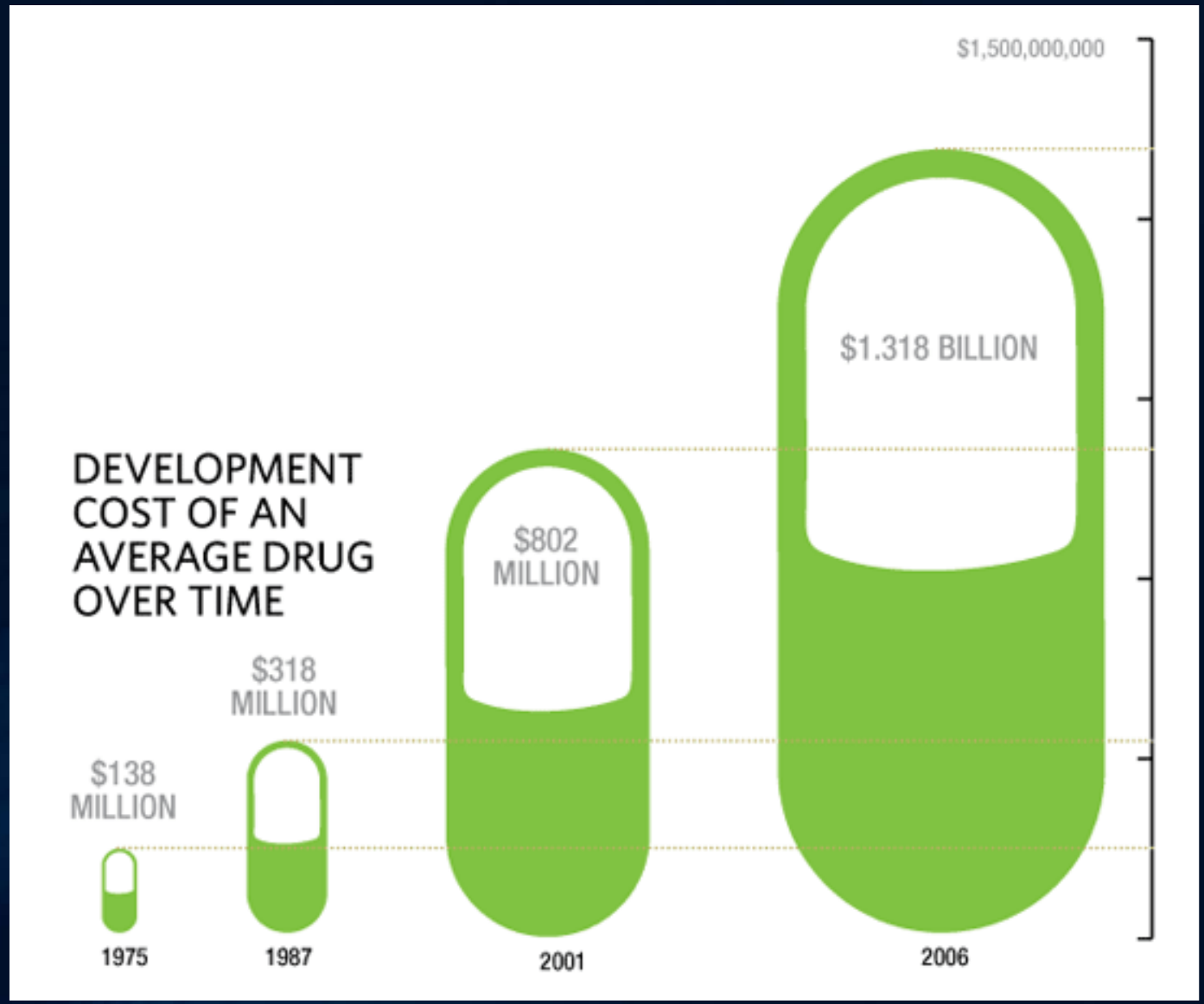
Drug Development Cost



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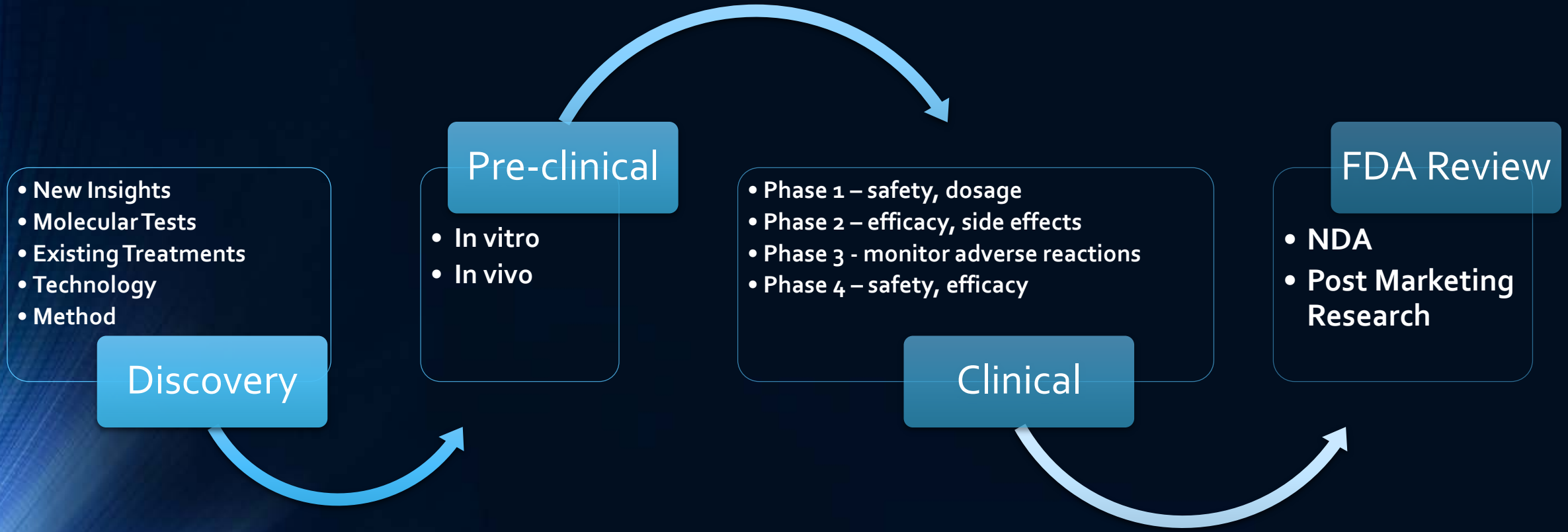
Drug Development Process



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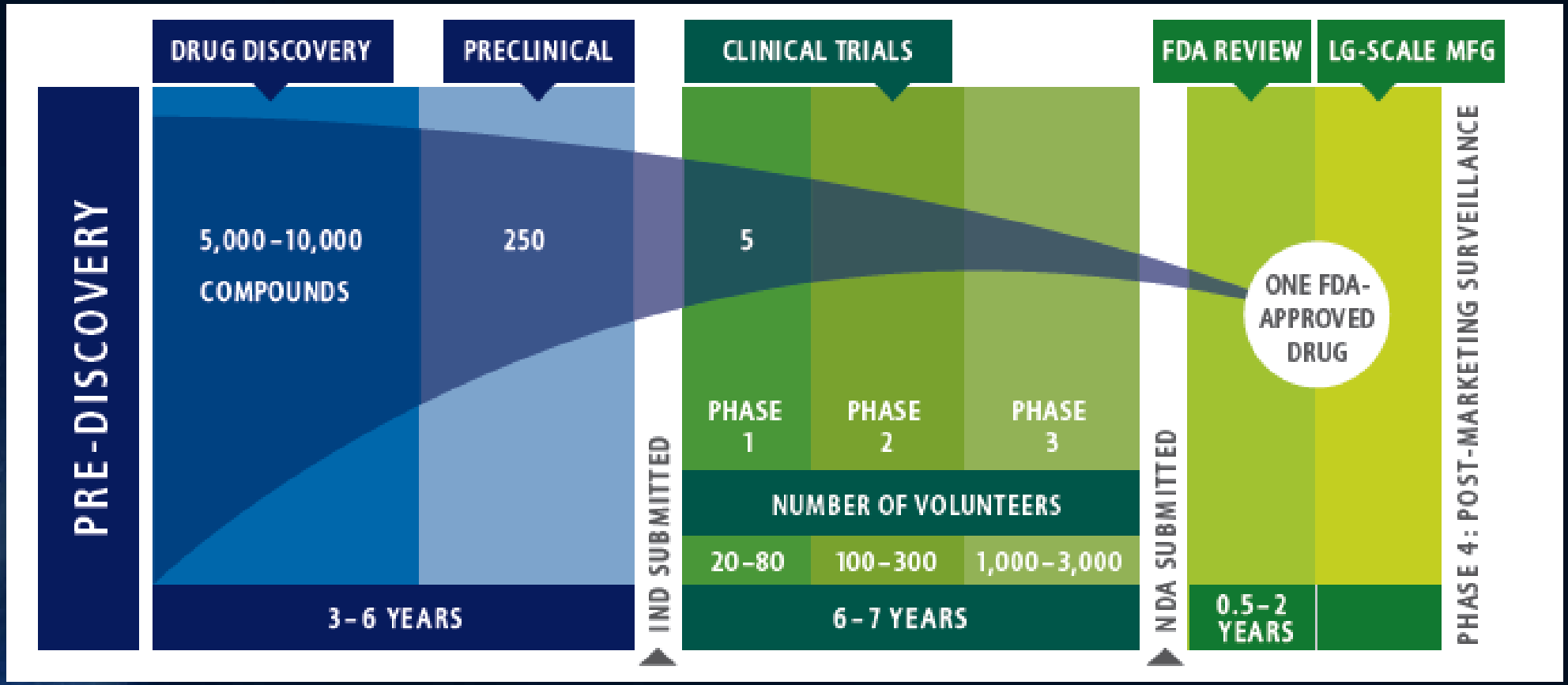
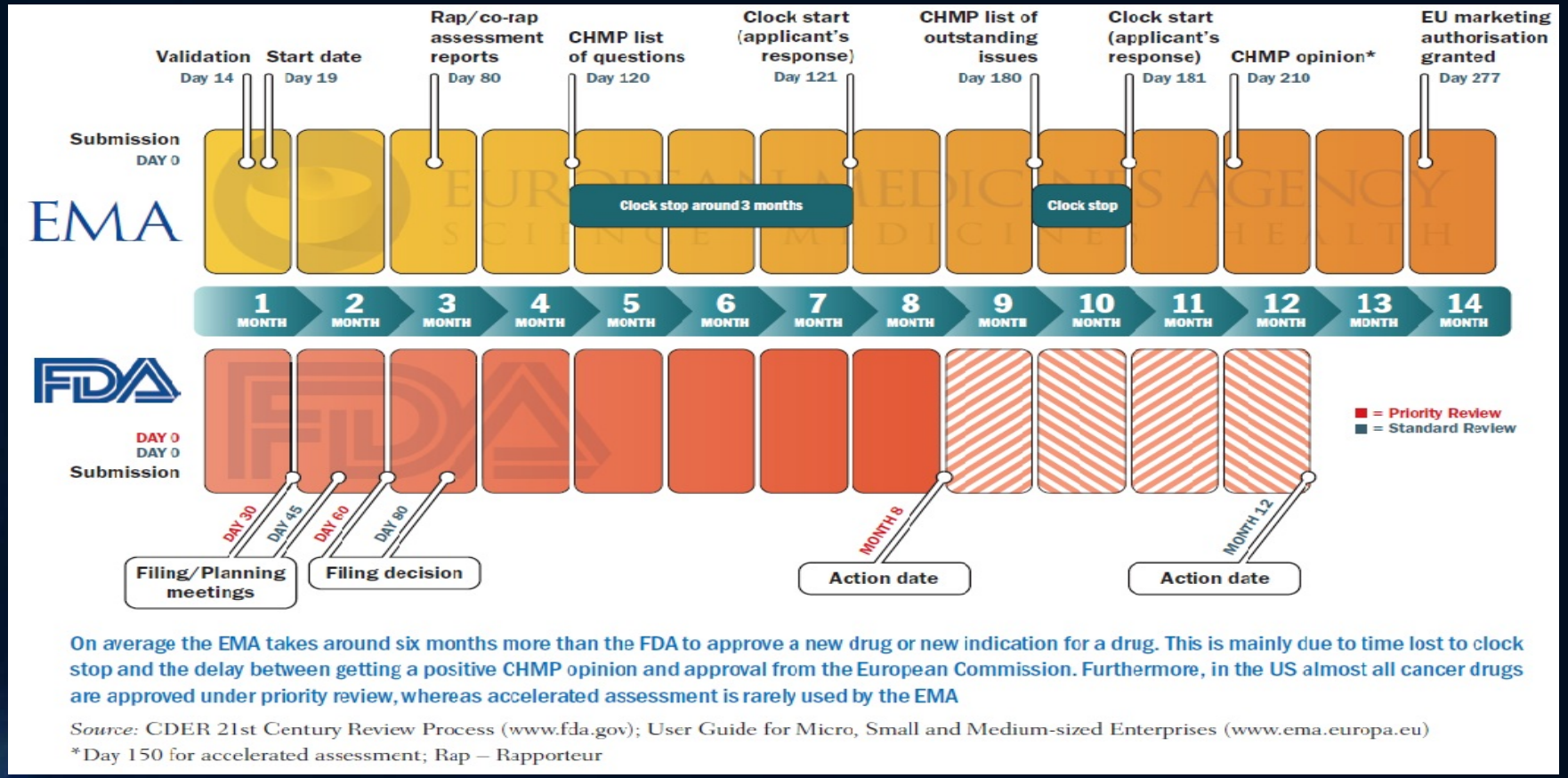
Drug Development Process



Drug Approval Process



On average the EMA takes around six months more than the FDA to approve a new drug or new indication for a drug. This is mainly due to time lost to clock stop and the delay between getting a positive CHMP opinion and approval from the European Commission. Furthermore, in the US almost all cancer drugs are approved under priority review, whereas accelerated assessment is rarely used by the EMA

Source: CDER 21st Century Review Process (www.fda.gov); User Guide for Micro, Small and Medium-sized Enterprises (www.ema.europa.eu)

*Day 150 for accelerated assessment; Rap – Rapporteur

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Obtaining Orphan Status (designation) www.fda.gov/orphan

Sponsor request statement	• Identified with specificity
Contact / Administrative Data	• If available: genetic and trade name, chemical name / descriptive name, source of drug
Rare Disease Description	• Proposed use of drug and why therapy is needed
Drug Description	• Characteristics and properties of pertaining elements, scientific rationale, in vitro data, clinical experience, etc.
Clinical superior explanation	• If needed
Orphan Subset	• Evidence if only a subset is medically plausible
Regulatory Status and Marketing History	• IND Status and marketing history
Population prevalence	• the disease/condition for which the drug is intended affects fewer than 200,000
References / Documentation	• Additional information

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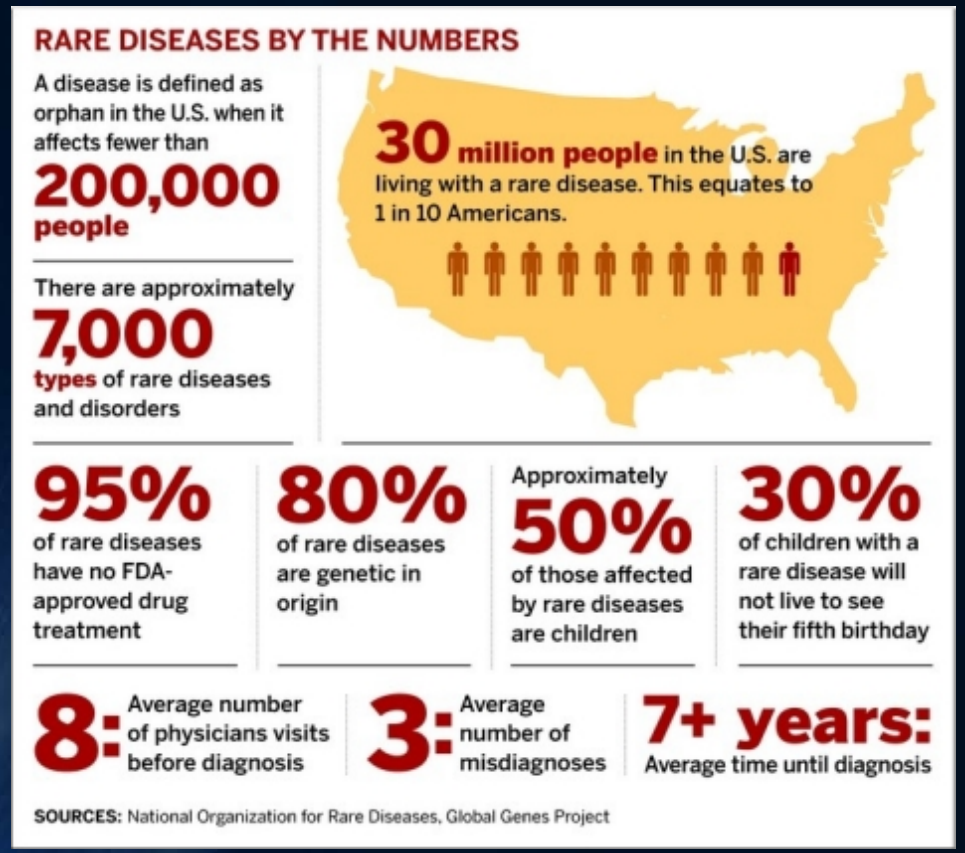
Rare Diseases



- 7000+ rare diseases and only ~500 to treat them
- Definition varies by country
  - What is rare in one country might not be rare in another
- Affects all body systems
  - Large % are genetic in origin
  - Range of Symptoms
    - Often lead to misdiagnosis
  - Rare diseases know no borders

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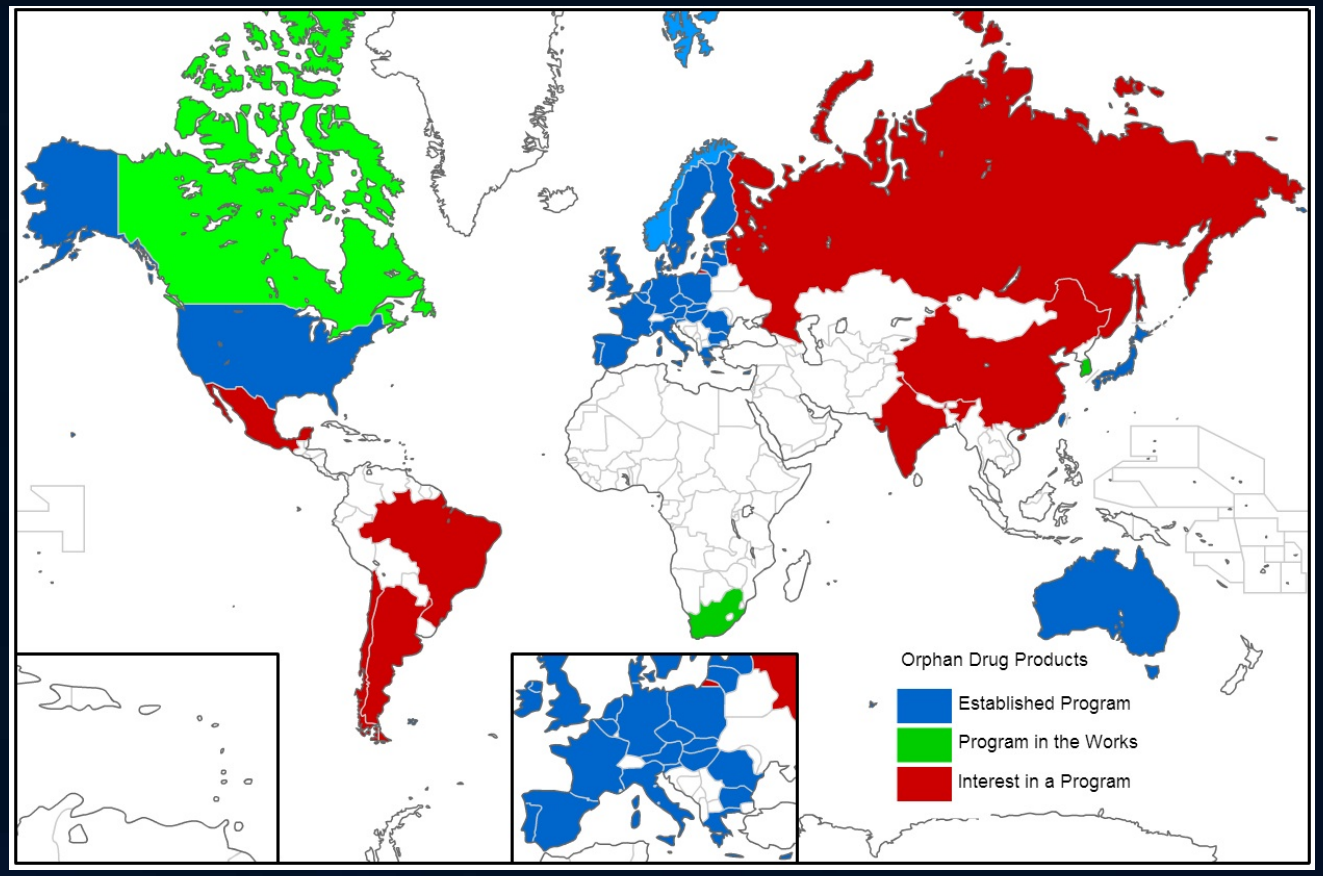
US Orphan Drug Act 1983

- Rare disease = prevalence < 200,000
- 7 Year Market Exclusivity
- FDA Filing Fee Wavier
- Tax Credits for clinical trials
- Orphan Product Grants
- ~502 drugs approved; >3400 designated (FDA)
- Use of accelerated approval/fast track/priority review/pediatric voucher

EU Orphan Drug Regulation 141/2000 (1999)

- Rare disease = prevalence < 5 per 10,000
- 10 Year Market Exclusivity (6 + 4 years)
- Must be Serious or Life threatening disease
- Tax credits by member state
- Grants via 8th Framework
- COMP designates – 38 members
- chair, 1 from each MS, 3 patient organization members, 3 from CHMP, 1 each Norway, Lichtenstein, Iceland, 1 from EC
- 864 designated; 68 approved orphan drugs
- approved 15 treatments for rare diseases in 2014 (37% of all drugs approved)

Rare Disease Legislation Around the World



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Challenges

- Natural History
  - Diagnosis
  - Prescribing/treatment practices
- Population Pool
  - Living in different parts of the world
- Effects in Variability
- Endpoints
- SAFETY!!!!

Opportunities

- Patient Advocacy
  - Social Media
  - Patient Groups
- Incentives
  - Monetary and Public Health
- Technology – Many new therapies were first approved as an orphan product
  - Gene Therapy – Glybera in the EU
  - Pegylation, liposomal encapsulation, lessons learned in cholesterol metabolism
- Changes in drug access - many
  - Fast Track
  - Priority Review
  - Accelerated Approval
  - Pediatric Voucher

Orphan Drug Landscape

- Orphan Drugs are "IN"
- Estimated worth of the global market - $50 Billion
- Percentage of orphan drugs with annual sales > 1 billion $ - 29%
- Percentage of orphan drugs with additional rare disease indications – 15%
- 452 Orphan products under FDA review in U.S. (2013)
- A record 260 orphan drug designations were granted in the US in 2014
- Same standards for review and approval as non-orphans "except" for FDA FLEXIBILITY

† - Sources: NORD, Orphanet, Evaluate Pharma, PhRMA, Thomson Reuters, FDA

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21st Century Cures Act - US

- House - Energy and Commerce; Ways and Means
- Increases funding for NIH and FDA
- Data Access
  - expand surveillance of neurological diseases
  - revise health information privacy rules
  - implement a system that allows further research on clinical trial data
- Orphan Product Extensions Now; Incentives for Certain Products for Limited Populations
  - Section 2151 - FFDCA is amended to extend market exclusivity by six months
  - Section 2152 - priority review voucher program
    - Extended for pediatric diseases through 2018
    - apply only to serious diseases
- Streamlining Clinical Trials
  - No consent required for medical devices that pose minimal risk
  - IRB reviews for clinical testing of medical devices no longer needs to be local

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Open Act HR971- US (analogous to 21st Centaury Cures)

- Proposed legislation from the senate
- Extends market exclusivity by 6 months for repurposed drugs that are approved to prevent, treat, or diagnose a new indication of rare disease
  - Requires indication from FDA on label
- Requires FDA to inform the public of products that receive 6 month extension
- Limits the product for one extension
- Applies only to new indications after the Act is passed
- Extension can be revoked only through untrue statements on application

Questions?

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