

# Insights into Rare Disease Drug Approval: Trends and Recent Developments

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**NORD Rare Diseases & Orphan Products Breakthrough Summit**  
October 17, 2017



# Disclosure

- I have no actual or potential conflict of interest in relation to this program/presentation.

## Orphan Drug Act

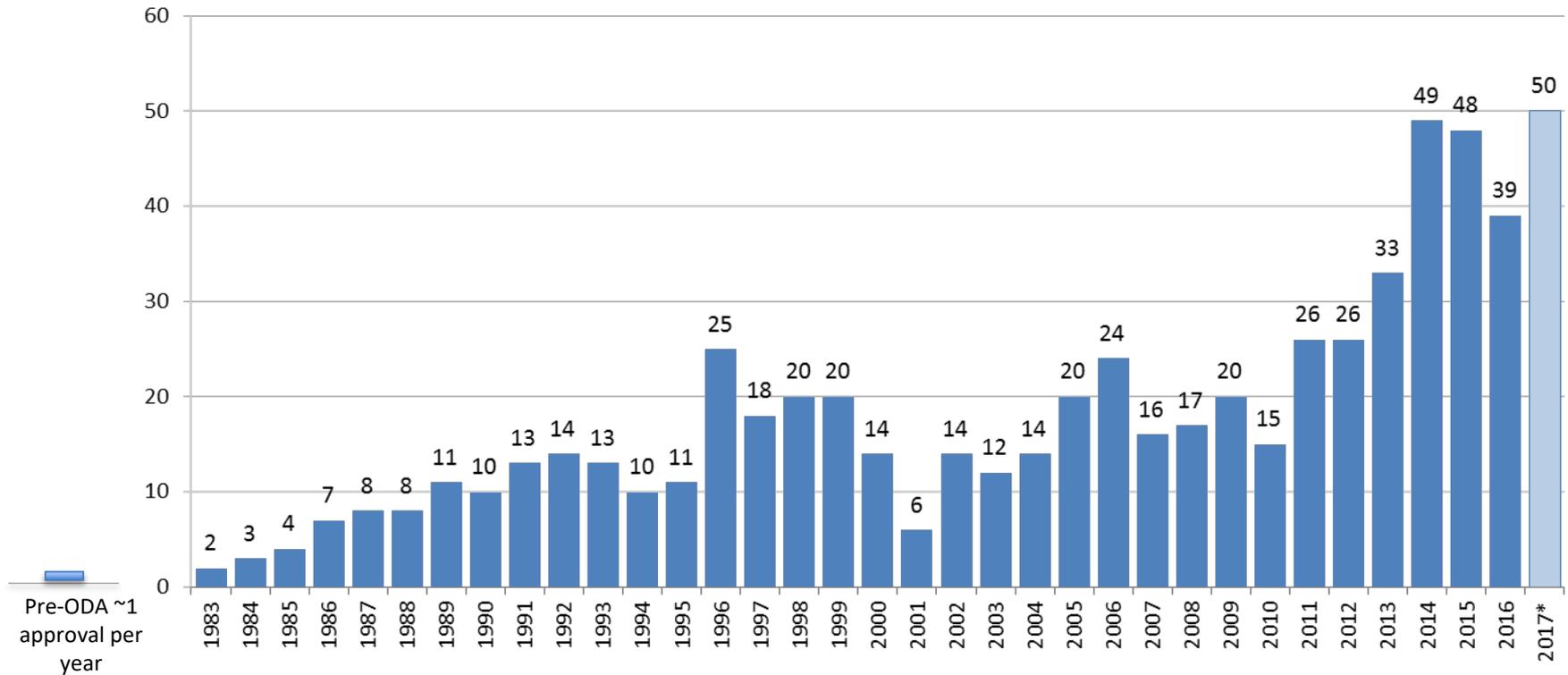
- The Orphan Drug Act was signed into law on Jan. 4, 1983
- Drug/biologic may be “designated” as an “orphan drug” if it is to prevent, treat, or diagnose a disease/condition that occurs in <200,000 patients in U.S.
- Designations are granted for a given drug for use in a given disease
- Incentives associated with designation:
  - Tax Credits – 50% **tax credit** for clinical research and testing expenses
  - **Waiver of User Fees**
  - 7 years of **marketing exclusivity** upon FDA approval of a specific orphan drug for a specific indication



# Orphan Drug Approval Trends

- In the decade leading up to the passage of the Orphan Drug Act, only 10 industry-supported products for rare diseases were brought to market
- Since 1983: 600+ **orphan drug indications** approved from 450+ **distinct drug products**

### Number of FDA Orphan Drug Approvals



“Product” defined as drugs having the same active ingredient and formulation

\*2017 figures of 9/15/2017

*“... our ultimate goal: to facilitate the development of safe, effective innovations that have the potential to meaningfully impact rare diseases.”*

**Scott Gottlieb, M.D.**

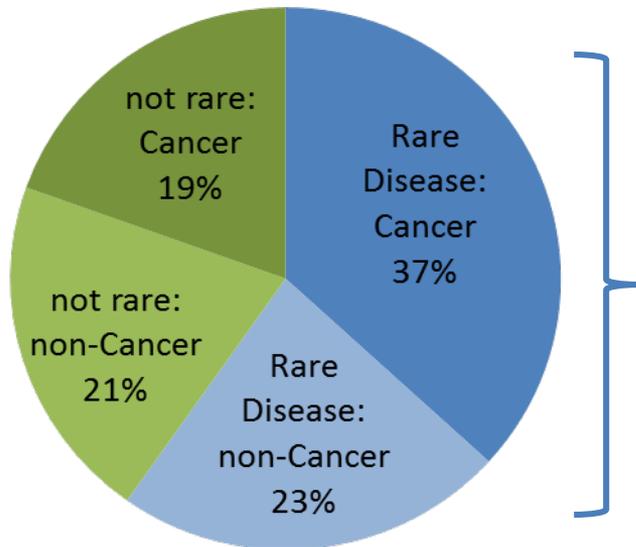
**Commissioner, Food and Drug Administration**

***FDA Voice Blog - 9/12/2017***

# Rare Disease and FDA's Breakthrough Therapy Designation Program

**Breakthrough Therapy Designation** : for drugs intended to treat a serious condition where preliminary clinical evidence indicates that the drug may demonstrate a substantial improvement over available therapies

**FDA Breakthrough Therapy Approvals Since 2013\***  
n = 87



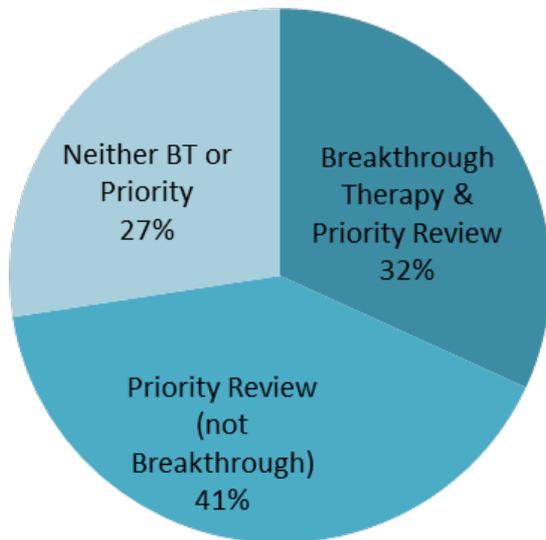
**60%** of the Breakthrough Therapies approved to date are indicated for Rare Disease

# Rare Disease and FDA's Priority Review Designation

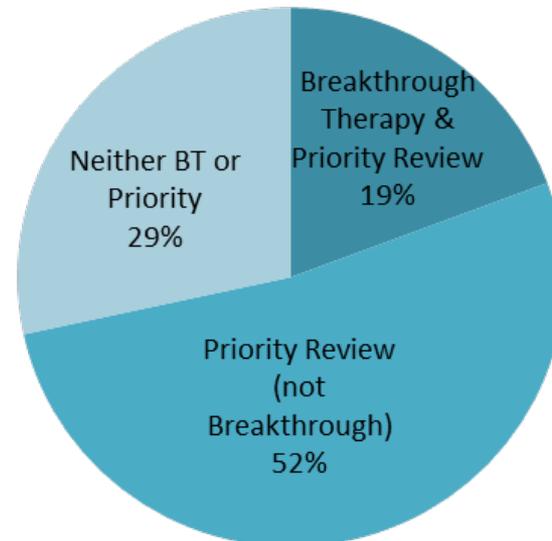
**Priority Review Designation** – granted to drugs which treat a serious condition AND, if approved, would provide a significant improvement in safety or effectiveness

## FDA Orphan Drug Approvals Since 2013\*

**Novel Drugs (n = 91)**



**New Indications (n = 88)**



Taken together over one-quarter of these orphan approvals received breakthrough therapy designation and nearly three-quarters received priority review

# 2017: A year of FDA “firsts” in Rare Disease



- tisagenlecleucel – First gene therapy approval in the United States
- avelumab - First FDA-approved treatment for metastatic merkel cell carcinoma
- lesipasvir + sofosbuvir - First HCV Direct-Acting Antivirals approved for use in adolescents
- cerliponase alfa - First FDA- approved treatment for a form of Batten disease
- edaravone - First new treatment for patients with ALS in over 2 decades
- ibrutinib – First FDA-approved therapy for the treatment of chronic graft-versus-host disease (GVHD)
- benznidazole - First treatment approved in the United States for the treatment of Chagas disease

“... For all the success of the ODA, there’s been criticism that some sponsors are using designations as a way to sidestep other important public health goals set out by Congress. We need to make sure our policies take notice of all of these new challenges and opportunities.”

**Scott Gottlieb, M.D.**  
**Commissioner, Food and Drug Administration**  
*FDA Voice Blog - 9/12/2017*

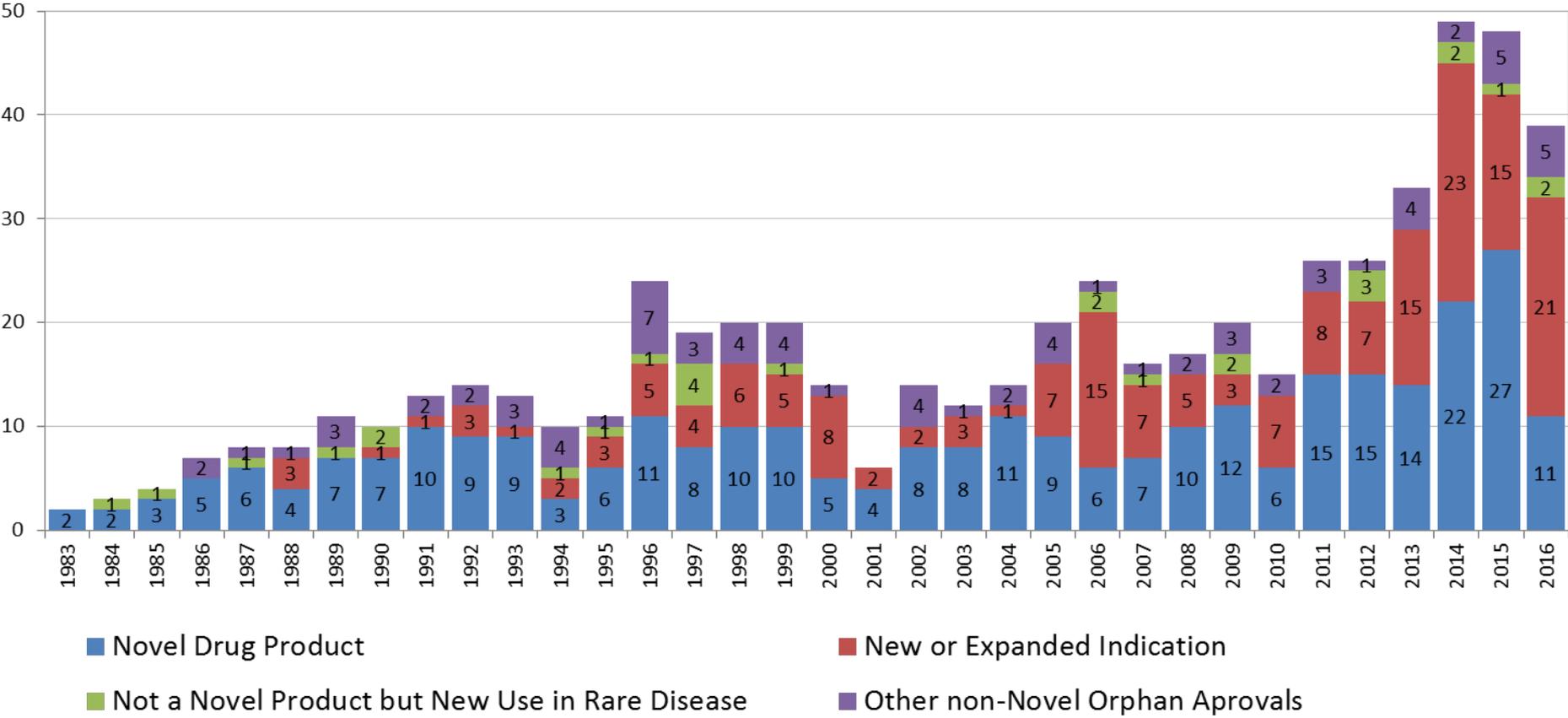
# Orphan Drug Approvals Over the History of the Program



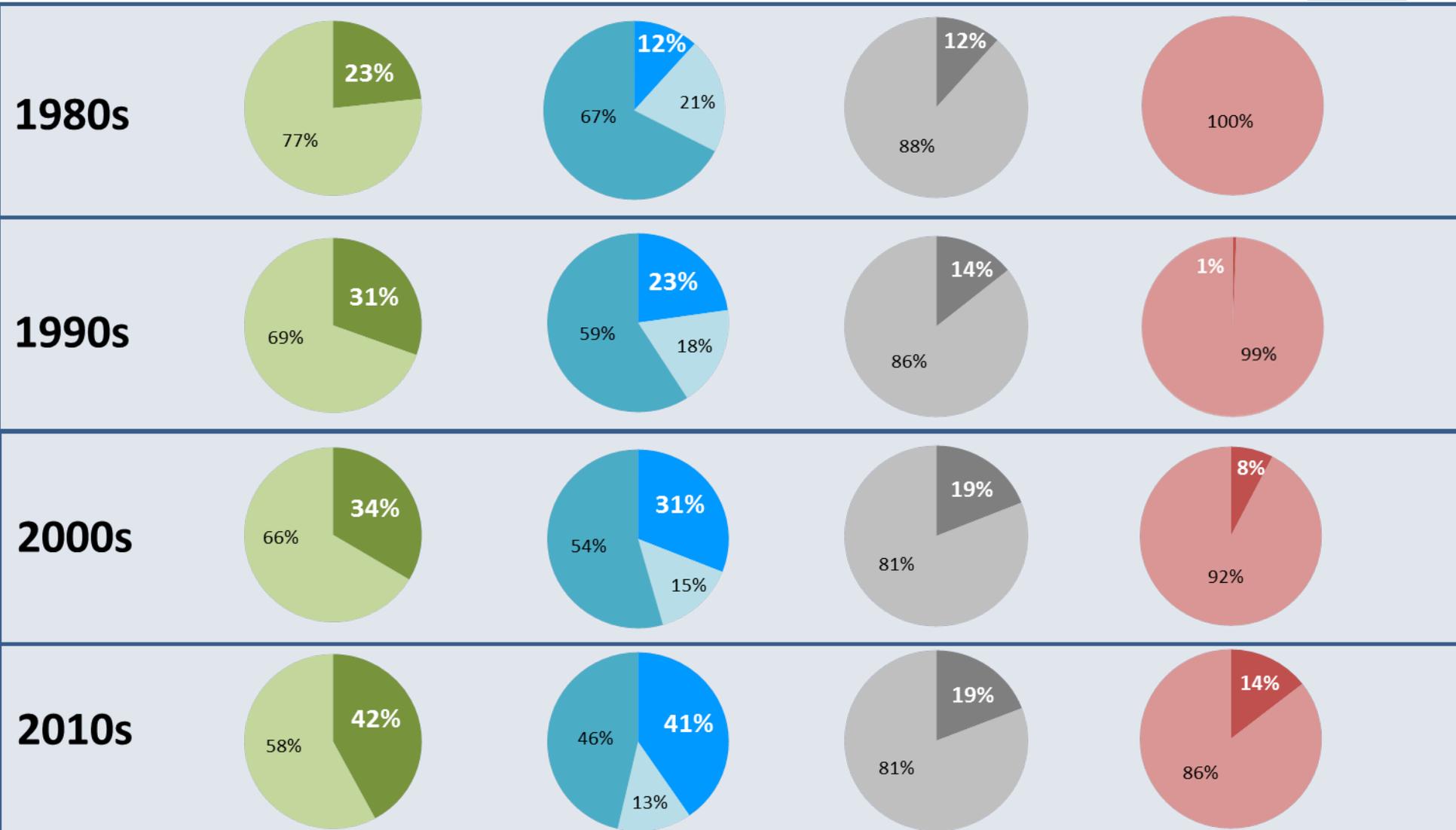
- All Orphan Drug **approvals** from the Office of Orphan Products Development (OOPD) Public Database from 1983 – 2016 (n = 590)
- Based on Trade name, active ingredient, and formulation, consolidated all orphan drug indication approvals into products (n = 451 distinct products)
- Researched the labeling and indication histories of all 451 products.
  - Classified whether the **initial** approval of each product was for rare or non-rare condition(s)
  - Identified the type of approval (novel drug, new indication, new formulation)
  - Identified whether or not the product **expanded** its indication post-approval and the history of those indication changes
  - Collected drug and disease characteristics data such as drug vs. biologic, therapeutic area, whether the drug was to treat a genetic condition, and whether the drug was a targeted therapy approved for a genetic or biomarker subset of a larger disease

# FDA Orphan Drug Approvals by Submission Type

- Both novel and new indication Orphan Drug approvals have increased in recent years.
- Pace of annual **novel** Orphan approvals has doubled since 2011.
- **New indication** approvals have greatly increased beginning in 2013.



# Orphan Drug Approval Characteristics Have Shifted Over Time

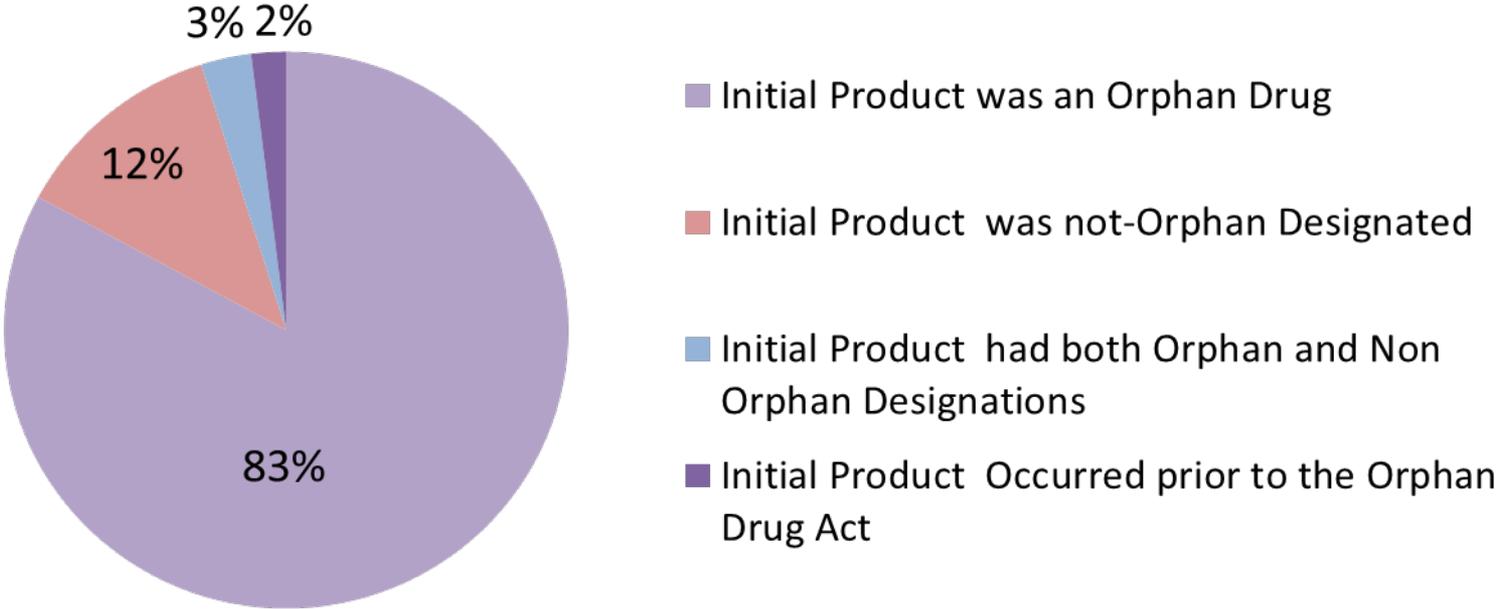


- Biologics
- Cancer
- Rare Genetic Disorder
- Targeted Therapy
- Small Molecule Drugs
- Metabolism and Endocrinology
- All Others
- Not Targeted

# When do Products Receive their First Orphan Approval?

- Over 80% of orphan drug products were **initially** approved as solely rare-disease treatments.
- Less commonly, a drug is first approved for marketing to treat a non-rare condition, but later adds one or more orphan indications.

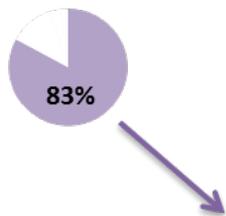
## 451 Distinct Products Receiving One or More Orphan Approval From FDA



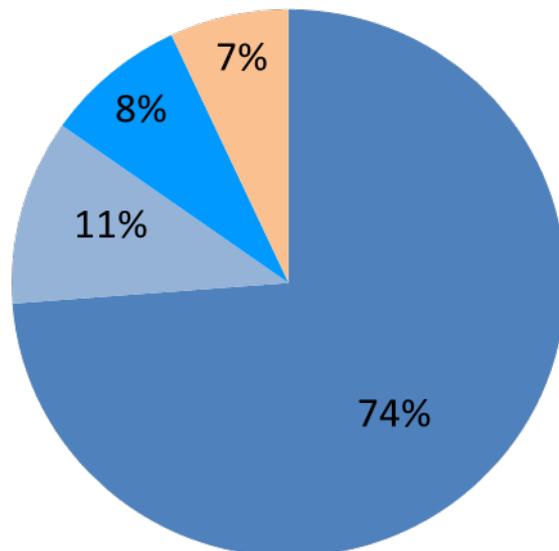
\* "Product" defined as drugs having the same active ingredient and formulation

# How Often Do Orphan Drugs Expand Approved Labeling to Treat Other Conditions?

- Nearly three-fourths of drugs initially approved as an orphan drug have **not** expanded their labeled indication.
- 85% of drugs approved for orphan diseases have **not** expanded to other conditions.
- Fewer than 10% of initial orphan approvals have added a non-rare indication to their label.



**New and Expanded Indications**  
**Initial Approved Product was an Orphan Drug**  
(n = 374)



- Have not expanded indication
- Expanded indication in same rare disease
- Added additional rare disease indication(s)
- Expanded the label to non-rare indication(s)

# Some High Revenue Drugs Have Orphan Indication(s)



Top Medicines by Invoice Spending			2012	2013	2014	2015	2016
Invoice Spending US\$Bn							
Total U.S. Market			317.8	331.5	378.5	425.3	450.0
1	Humira	Orphan Drug Approval	4.5	5.7	7.8	10.7	13.6
2	Harvoni		0.0	0.0	1.6	14.3	10.0
3	Enbrel	Orphan Drug Approval	4.2	4.9	5.9	6.6	7.4
4	Lantus Solostar		2.3	3.3	4.8	5.8	5.7
5	Remicade	Orphan Drug Approval	3.8	4.1	4.5	5.0	5.3
6	Januvia		2.6	2.9	3.5	4.2	4.8
7	Advair Diskus		4.6	5.0	4.7	4.7	4.7
8	Lyrica		1.9	2.4	3.1	3.8	4.4
9	Crestor	Orphan Drug Approval	4.8	5.3	5.7	6.3	4.2
10	Neulasta	Orphan Drug Approval	3.4	3.6	3.8	4.1	4.2
11	Copaxone	Orphan Drug Approval	3.5	3.8	4.0	4.4	4.1
12	Rituxan	Orphan Drug Approval	3.1	3.3	3.5	3.7	3.9
13	Tecfidera		0.0	1.0	2.9	3.5	3.7
14	Xarelto		0.3	1.1	2.1	2.8	3.6
15	Lantus		2.2	2.6	3.5	3.8	3.3
16	Eliquis		0.0	0.1	0.6	1.6	3.2
17	Truvada		2.1	2.1	2.4	2.8	3.1
18	Vyvanse		1.6	1.9	2.2	2.6	3.1
19	Avastin	Orphan Drug Approval	2.6	2.7	2.9	3.1	3.1
20	Symbicort		1.2	1.5	2.2	2.7	3.0

- Majority of these examples of top selling orphan drugs are products that were first approved to treat **non-rare** diseases.

**Key:**

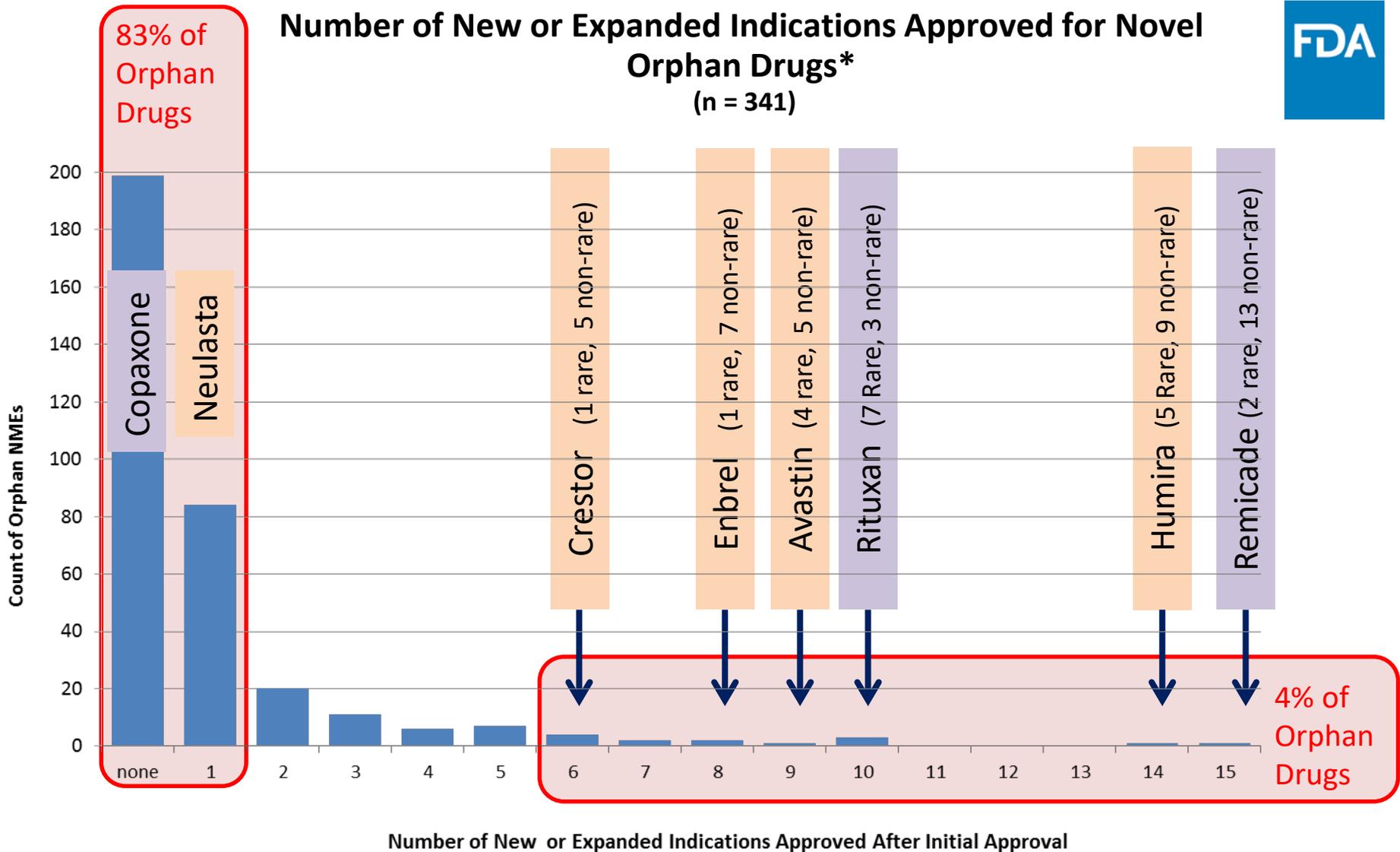
Initial Approval Orphan Drug

Initial Approval **not** Orphan

## Question:

**Do these highest-revenue orphan drugs expand their labeled indications similar to other orphan drugs?**

# Number of New or Expanded Indications Approved for Novel Orphan Drugs\* (n = 341)



Most of the highest-revenue orphan drugs received a much greater number of expanded indication approvals than is typically experienced with orphan drugs.

\*All Novel Orphan Drugs included, regardless of whether the initial approval was orphan or not

## Closing Thoughts

- The Orphan Drug Act has been a successful catalyst in spurring valuable rare disease drug development.
- The number of orphan drug approvals have increased in recent years. Both novel agents and new indications serve as the primary drivers of this recent orphan drug growth.
- The high proportion of these approvals qualifying for priority review and/or breakthrough therapy designation suggest the potential of orphan drug approvals to positively impact the rare diseases they treat.
- Biologics, rare cancer treatments, and targeted therapies are reflected in a growing proportion of orphan drug approvals over time.
- Most products receiving an orphan approval start out as rare disease treatments, and do not expand their use to non-rare conditions.
- Reflecting on past successes and being mindful of recent changes are important ways that we can help ensure that policies continue to support meaningful innovation for patients facing rare diseases.

