Rare Disease Legislation: A Historical Primer

Orphan Drug Act:

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Priority Review Vouchers:

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The Orphan Drug Act

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Associate Director of Public Policy
Our Vision

NORD’s vision and guiding principles on which our advocacy initiatives are based:

- A national awareness and recognition of the challenges faced by people living with rare diseases and the associated costs to society.
- A nation where people with rare diseases can secure access to diagnostics and therapies that extend and improve their lives.
- A social, political, and financial culture of innovation that supports both the basic and translational research necessary to create diagnostic tests and therapies for all rare disorders.
- A regulatory environment that encourages development and timely approval of safe and effective diagnostics and treatments for patients with rare diseases.
Major NORD Programs and Initiatives

- Policy and regulatory advocacy
- State advocacy and alliance partnerships
- Patient representation (FDA, NIH, SSA)
- Education (patients, professionals, public)
- Mentoring (patient organizations)
- Patient assistance programs
- Patient Networking (disease specific meetings, online communities, creation of new patient organizations)
- Increase disease understanding (Research grants, patient registries)
- International Partnerships
- US Sponsor of International Rare Disease Day
The Orphan Drug Act of 1983
The Orphan Drug Act

In the decade before 1983, only 10 new treatments were brought to market by industry for diseases that today would be defined as rare.

A total of 34 orphan therapies approved by the FDA
The Orphan Drug Act

- Leaders of rare-disease patient organizations began to realize that there were certain problems their patients and families shared...problems that were common to all people with rare diseases.
The Orphan Drug Act

- On January 4th, 1983, the Orphan Drug Act was signed by President Ronald Reagan.
The Orphan Drug Act

What is in the Bill?
The Orphan Drug Act

• Orphan Drug Designation:
  – First, the drug must meet the qualifications of:
    • Section 505 of the FD&C Act (small molecule drugs)
    OR
    • Section 351 of the Public Health Services Act (large molecule biologics)
The Orphan Drug Act

• Orphan Drug Designation:
  – FDA determines whether the drug is “intended to treat a rare disease or condition”.
  – Defined by:
    • “Affects less than 200,000 people in the U.S.
    • “Affects more than 200,000 people in the U.S., but there is no reasonable expectation a company will recover costs through sales”
The Orphan Drug Act

• Once approved, seven years of exclusivity
  – The FDA grants 7 years of exclusivity to the drug
  • The FDA cannot approve the “same drug” from another company, unless:
    – The patent holder cannot supply the drug
    – The patent holder consents to the other company’s development of the drug
The Orphan Drug Act

• Other provisions:
  – The Orphan Products Grant Program
    • “The goal of the Orphan Products Grants Program is to encourage clinical development of products for use in rare diseases or conditions. The products studied can be drugs, biologics, medical devices, or medical foods.”
    • –FDA Office of Orphan Product Development
    • Approximately $14 million in grants per year
The Orphan Drug Act

• Other provisions:
  – The Orphan Products Grant Program since 1983 has:
    • Received over 1800 applications
    • Reviewed over 1400 applications
    • Funded over 500 studies
    • 45 drugs on the market originated from the Orphan Grants Program
The Orphan Drug Act

• Other provisions:
  – Orphan Products Board:
    • Coordinating body made up of:
      – Patients
      – Governmental Agencies
      – Pharmaceutical Companies
      – Insurers
      – Physicians
      – Others
The Orphan Drug Act

• Other provisions:
  – Orphan Drug Tax Credit (ODTC):
    • Allows companies to claim a tax credit of up to 50% of their qualified clinical testing expenses.
    • Not all companies opt to take the ODTC, instead choosing to take the R&D credit
The Orphan Drug Act

Estimated Decline in Investment in Orphan Drugs by Developer Type in the Absence of the ODTC

-40% -35% -30% -25% -20% -15% -10% -5% 0% -5% -10% -15% -20% -25% -30% -35% -40%

Established Pre-market Total

Property of NORD
The Orphan Drug Act

• Other provisions:
  ▪ Exemption from user fees (Added in 1992)
    ▪ FY2016 User Fees –
      ▪ $2,374,200 for an application requiring clinical data
      ▪ $1,187,100 for an application not requiring clinical data or a supplement requiring clinical data
      ▪ $585,200 for an establishment
      ▪ $114,450 for a product
The Orphan Drug Act

Figure 3. Available ODA assistance during development timeline for orphan drugs

- Orphan Product Grant Program
- Orphan Drug Tax Credit
- Market exclusivity
- Investigational New Drug Application
- New Drug Application (fee waiver)

Timeline:
- New drug discovery: 52 months
- Preclinical testing: 82 months
- Clinical trials (Phase I, II, III): 16 months

Average 12.5 years

The Orphan Drug Act

• Has it worked? Yes!
  – Before 1983:
    • 10 orphan therapies developed by industry
  – Since 1983:
    • Over 450 orphan therapies developed by industry, with more than 1,000 orphan therapies currently in the pipeline
The Orphan Drug Act

• Has it worked? Yes!

Figure 1. New orphan drugs before and after the ODA

Note: New orphan drugs are defined as NMEs or BLAs. Prior to the ODA, the graph shows the average annual number of approved drugs that would have been considered orphan drugs.
Source: Drug Approval Reports, Food and Drug Administration, various years; EY analysis.
Thank You!

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Rare Pediatric Disease Priority Review Vouchers
Rare Pediatric PRV - Overview

• **Purpose** – Additional Incentive for companies to develop therapies for rare pediatric diseases.

• **Why Needed? Original Setting?** – By 2011, even though incentives of Orphan Drug Act in effect since 1983, during almost 3 decades, only 1 drug approved to treat childhood cancer vs. 50 for adults. Many other rare pediatric diseases were similarly without treatments -- needed additional incentives to develop treatments for kids with rare diseases.

• **Legislators & Advocates Act** – With strong support from patient advocates such as those representing childhood cancer, Every Life Foundation, NORD, as well as children’s hospitals and industry, etc., members of house and senate decided to act.
Rare Pediatric PRV - Overview

• **Result** - Reps. McCaul (R-TX), Butterfield (D-NC), Myrick (R-NC) & Van Hollen (D-MD) joined by impressive list of bipartisan House co-sponsors to introduce Creating Hope Act of 2011 (modeled on Tropical Disease PRV in place since 2007). Senators Casey (D-PA) & Brown (R-MA) & 11 Senate co-sponsors offered the Senate counterpart bill. The Creating Hope Act was signed into law in 2012 as part of package that is legislated every 5 years.

• **How it Works** – company that successfully develops therapy for rare pediatric disease can, upon approval, apply for priority review voucher that entitles holder to FDA review of another therapeutic candidate in 6 months of submission of application for approval rather than the standard 10 months.
Rare Pediatric PRV - Overview

• So, how does that incentivize development of RPD treatments when we know that all applications for approval of a rare disease therapy get the priority, 6-month review already? The company that is issued a voucher can sell the voucher to a company that can use it for common disease application.

• How much difference to the purchasing company? HUGE! Companies developing treatments for common diseases are in super competitive space in which they enjoy tremendous financial advantage by being first to the market. So, if they can secure a voucher that provides them with review of their application in 6 months while competitors must wait 10 months or more, that is of tremendous value. Does not improve prospect of approval but improves prospect of getting to the market faster.
Rare Pediatric PRV – Experience to Date

• **How much incentive for rare disease developer? HUGE! Why?**
• FDA has issued 6 RP PRVs.
• **Sales** – BioMarin to Sanofi and Regeneron for $67M (used successfully for cholesterol drug Praluent); Retrophin to Sanofi for $245M (redeemed Dec. 2015 in NDA for type 2 diabetes); United Therapeutics to AbbVie for $350M (plans unknown).
• So, can see that companies successful in developing a therapy for a rare pediatric disease can sell their voucher for a lot of money they can spend in developing another such therapy. This is an especially important incentive for smaller companies and for their investors.
• Another beauty is that the money is not taxpayer dollars!
Rare Pediatric PRV – Currently in Play

• **Issue 1 – Sunset Provision** – Legislation included a “termination” clause – no RP PRVs to be issued after 1 year following issuance of 3rd PRV (issued March 17, 2015, so sunset was to be March 17, 2016). But, combined approps bill for 2016 extended sunset to Sep. 31, 2016.

• **Advancing Hope Act** – Sponsors of Creating Hope Act, anticipating sunset next month, offered Advancing Hope Act – would delete the termination/sunset clause.

• **21st Century Cures Act** (House HR 6) – includes Advancing Hope Act but would reset sunset to Dec. 31, 2018.

• **Senate Action** – Committee on Health, Education, Labor & Pensions (HELP) considering legislation dealing with some provisions of 21st CCA; scheduled to consider RP PRV in committee hearing on March 9.
Rare Pediatric PRV – In Current & Future Play

• **Issue 2- Disease Eligibility** – Current law reads:

  • The term ‘rare pediatric disease’ means a disease that “primarily affects individuals aged from birth to 18 years, including age groups often called neonates, infants, children, and adolescents, ... and is a rare disease or condition. Seems clear but FDA draft guidance and current policy adds, “which we interpret as meaning that greater than 50% of the affected population in the U.S. is aged 0 through 18 years.”

  • This interpretation excludes diseases in which patients are severely affected as children but a large number of them survive their 18th birthday although at a greatly reduced quality of life and with greatly reduced treatment window because so much of the disease damage is already done. Important to many PGs and industry – submitted comments.
Rare Pediatric PRV – FDA Concern

• **Issue 3 – FDA Concern** – This more restrictive interpretation and FDA’s misgivings about the voucher program are understandably based on the concern that, if too many vouchers were issued, the FDA could face a deluge of applications for approval of therapies for common diseases that would need to be given priority reviews (within 6 months) and the Agency would not have sufficient resources and staff to process them that quickly.

• But, existing law and current proposals contain restrictions intended to limit the number of vouchers: drug can contain no active ingredient previously approved; app must rely on clinical data in pediatrics & at doses intended for pediatrics; does not seek approval for adult indication. Also, only 6 vouchers issued in first 3 years & PRVs have > user fees.
Rare Pediatric PRV – Going Forward

• You can see the vouchers program is a complicated attempt to create additional incentives for developing treatments for rare pediatric diseases.

• You might want to keep an ear out for what the Senate decides to do regarding the program and for the final product of the eventual Senate-House conference committee.

• Depending on what the final legislation contains once enacted; depending on any draft guidance the FDA issues regarding the program, & depending on how your particular disease group is affected, you might want to consider, at the appropriate time, making your views and comments known.

• Thank you for your attention.

• Questions or comments?
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