FDA Incentives

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Orphan Product Related Incentives

- Orphan Products Grants Program
- Tax Credits
- Waiver of Marketing Application User Fees
- Orphan Drug Exclusivity

Other FDA Incentives

- Rare Pediatric Disease Priority Review Voucher
- Neglected Tropical Disease Priority Review Voucher
- Generating Antibiotics Incentives Now (GAIN)
- Breakthrough Designation

ORPHAN PRODUCT RELATED INCENTIVES

Orphan Products Grants Program

- Competitive grant program
  - Drugs, biologics, medical devices, or medical foods
  - ~$14 million dollars per year
  - $200- $400K/year for 3 or 4 years, then re-compete
  - Domestic or foreign, public or private, for-profit or nonprofit entities
  - Request for Application (RFA) available on website

ORPHAN DESIGNATION STATUS RELATED INCENTIVES

Tax Credits

- Equal to 50% of clinical trial costs
- Can be applied to Federal taxes incurred in prior year (1-year carry back) or applied for up to 20 years (carry forward) against future taxes
- Administered by Internal Revenue Service (IRS)

Marketing Application User Fee Waiver

Orphan-designated drugs/biologics may apply for an exemption from Prescription Drug User Fee Act (PDUFA) marketing application fees

- FY 2012: $1.84 million
- FY 2013: $1.96 million
- FY 2014: $2.17 million

Orphan Drug Exclusivity

- Receive Orphan Drug Designation
- The first sponsor to receive marketing approval for that drug for that indication

  -7 years of exclusivity following FDA market approval

  FDA cannot approve same drug for same indication during exclusivity period

Orphan Drug Exclusivity

- Sponsor of the "same drug" as an ***already approved drug***
  - For Designation – Must provide a plausible hypothesis of clinical superiority
  - For Orphan Exclusivity – Must demonstrate the drug is clinically superior

Orphan Drug Exclusivity

If Orphan Drug Designation is based on a plausible hypothesis of clinical superiority for greater efficacy or safety clinical superiority must be demonstrated at the time of marketing approval in order to receive Orphan Drug Exclusivity.

- **May require head to head trials**.

Orphan Drug Exclusivity

Clinical Superiority Examples Where Head to Head Trials Were NOT Required

Safety:

-Immunogenicity

- Japanese encephalitis vaccine, inactivated, adsorbed (JE-NS vs. JE-Gelatin)

-Changing salt or ester

- Glycerol Phenylbutyrate vs. Sodium Phenylbutyrate

-Recombinant

- Recombinant Factor VIII vs. Factor VIII

Orphan Drug Exclusivity

Efficacy:

- Head to head trials are required to demonstrate greater efficacy and sponsors are reluctant to do these.

Orphan Drug Exclusivity

If Orphan Drug Designation is based on a plausible hypothesis of clinical superiority based on a Major Contribution to Patient Care (MC-PC) the product is eligible for Orphan Drug Exclusivity

MC-PC Examples

- Oral formulation of a previously approved intravenous drug
- Cysteamine, enteric coated (q 12h) vs. Cysteamine (q 6h)
  (data showed that strict adherence to q6h dosing was required for therapeutic effect)

Other FDA Incentives

Rare Pediatric Disease Priority Review Voucher

Rare Pediatric Disease Priority Review Voucher (PRV)

- Created under FDA Safety and Innovations Act (FDASIA) to encourage development of drugs and biologics for "rare pediatric diseases"
  - Section 529 of the Food, Drug, & Cosmetic Act
- Basic Idea: If a sponsor receives approval of a **"rare pediatric disease product application"** for a **"rare pediatric disease,"** the sponsor is eligible to receive a PRV which can be redeemed, or transferred to another sponsor, to obtain priority review of another application that would otherwise be ineligible for priority review
  - Modeled after the Tropical Disease Priority Review Voucher

Rare Pediatric Disease PRV (cont.)

- "Rare Pediatric Disease"
  - "Primarily affects individuals from birth to 18 years" AND
  - Is a "rare disease or condition" (includes diseases /conditions that affect fewer than 200,000 in the US)

- "Rare Pediatric Disease Product Application"
  - NME (New Molecular Entity)
  - Regulated under 505(b)(1) or 351(a)
  - Eligible for priority review
  - Relies on clinical data from studies in a pediatric population
  - Does not seek approval for an adult indication

Rare Pediatric Disease PRV (cont.)

- Consists of 2 components:
  - Designation as a "rare pediatric disease"
    - Voluntary
    - Not a pre-requisite to be eligible for a PRV
    - Administered by OOPD
  - Determination of voucher eligibility
    - Whether NDA or BLA satisfies criteria for a "rare pediatric disease application"
    - Administered by individual review divisions in CDER & CBER
    - If designation not sought, OOPD consulted as to whether disease is a "rare pediatric disease"
- Sunset provision

Rare Pediatric Disease PRV (cont.)

5 Rare Pediatric Disease Designation Requests Received

3 Rare Pediatric Disease Designations Granted

1 Rare Pediatric Disease PRV Issued

- Elosulfatase alfa -treatment of mucopolysaccharidosis IV A (Morquio A Syndrome)

TROPICAL DISEASE PRIORITY REVIEW VOUCHER

Tropical Disease PRV

- Created in 2007 under FDAAA to encourage the development of drugs and biologics to prevent and treat tropical diseases
  - Not limited to rare diseases

- Same basic idea as the Rare Pediatric Disease PRV:
  - If a sponsor receives approval of a **"tropical disease product application"** for a **"tropical disease,"** the sponsor is eligible to receive a PRV which can be redeemed, or transferred to another sponsor, to obtain priority review of another application that would otherwise be ineligible for priority review

Tropical Disease PRV

- "Tropical Disease"
  - Statute enumerates a list of diseases that qualify

Key difference with Rare Pediatric Disease PRV

- "Tropical Disease Product Application"
  - NME
  - 505(b)(1) or 351(a)
  - Eligible for priority review

Similar to Rare Pediatric Disease PRV

List of Tropical Diseases

1. TUBERCULOSIS	9. HUMAN AFRICAN TRYPANOSOMIASIS
2. MALARIA	10. LEISHMANIASIS
3. BLINDING TRACHOMA	11. LEPROSY
4. BURULI ULCER	12. LYMPHATIC FILARIASIS
5. CHOLERA	13. ONCHOCERCIASIS
6. DENGUE/DENGUE HEMORRHAGIC FEVER	14. SCHISTOSOMIASIS
7. DRACUNCULIASIS (GUINEA-WORM DISEASE)	15. SOIL TRANSMITTED HELMINTHIASIS
8. FASCIOLIASIS	16. YAWS

- FDA to add to this list by regulation

Rare Pediatric Disease PRV vs. Tropical Disease PRV

RARE PEDIATRIC DISEASE PRV	TROPICAL DISEASE PRV
Defines "rare pediatric disease" and allows for a case by case determination • No list	List of tropical diseases with ability to add via rulemaking
No limits on transferability	Only one transfer permitted
Notify FDA 90 days before redeeming voucher	Notify FDA 1 year before redeeming voucher
Sunset provision	No sunset provision

Tropical Disease PRV

2 Tropical Disease PRVs Issued

- Artemether/lumefantrine – malaria
- Bedaquiline- tuberculosis

Generating Antibiotic Incentives Now (GAIN)

GAIN Act

- Created under Title VIII, Section 801 of FDASIA 2012
- Aims to encourage development of antibacterial and antifungal drugs for the treatment of serious or life threatening infections
- Eligible product is granted Qualified Infectious Diseases Product (QIDP) designation

GAIN Incentives

- **Additional 5 years exclusivity** granted at the time of approval for products that have been granted a *Qualified Infectious Disease Product* designation

- **Priority review** for marketing applications for products that have a QIDP designation

- Products that have been granted a QIDP designation are eligible for **fast track** designation

Breakthrough Therapy Designation

Breakthrough Therapy Designation

- Created under Section 902 of FDASIA
- Aims to expedite development and review of breakthrough therapies

Breakthrough Therapy Designation

Qualifying Criteria:

- A drug that is intended to treat a serious or life-threatening condition

AND

- Preliminary clinical evidence indicates that the drug may demonstrate substantial improvement on 1 or more clinically significant endpoints over available therapies

Breakthrough Therapy Designation

- Intensive guidance on efficient drug development during IND, beginning as early as Phase 1

- Organizational commitment involving senior manager

- Approval may be based on an effect on a surrogate or intermediate clinical endpoint that is reasonably likely to predict a drug's clinical benefit

- Shorter clock for review of marketing application (6 months compared to the 10-month standard review)

Breakthrough Therapy Designation

Additional consideration:

- Designation may be withdrawn if it no longer meets breakthrough therapy qualifying criteria

Contact Information

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ORPHAN PRODUCTS DEVELOPMENT

Thank You