Considerations for Global Development of Orphan Drugs

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Drug Development and Regulation is Global

- Most drug development companies operate globally
  - Clinical trials conducted globally
  - Drug products registered throughout the world
- Health authorities continue to develop globally
  - Formerly the established health authorities included ICH (Japan, US, EU) and other major countries (Canada, Australia, and others)
  - Increasing growth and sophistication of health authorities throughout the world

Global Environment for Rare Diseases

- US instituted the first rare disease program
  - Orphan Drug Act of 1983
  - Hugely successful
  - Based on incentives and rewards for orphan drug development
- Japan developed the second program in 1993
- Europe instituted a program in 2000

Health Authority Programs for Orphan Diseases

- Australia – program started in 1998, worked closely with US FDA to develop
- Thailand – program instituted in 2007
- Taiwan – program instituted in 2010
- Korea - program instituted in 2004

Latin America

- Columbia
- Mexico (pending)
- Argentina
- Equador
- Peru
- Panama

- Brazil – Possible fast track for rare disease products based on unmet medical need

Russia

- Russia enacted a Health Care Law In November 2011
  - Defines Rare Diseases as life-threatening or chronic progressing diseases that result in life expectancy decrease or permanent disability in less than 1 patient per 10,000 people
  - Ministry of Health will define conditions that qualify in the Federal Registry (86 rare diseases currently; 24 diseases qualify for federal support)

Middle East

- No formal ODD process in Egypt, Israel, Lebanon, and Saudi Arabia

- In Israel, drugs that are imported and are classified as orphan drugs in their country of origin, and produced or imported into Israel in small quantities, may be considered “rare and expensive” drugs. The Ministry of Health may exercise some regulatory discretion with the products.

Asian Countries

- Several countries do not currently have a formal orphan drug program in place, but allow for expedited review of orphan drugs

  - China (some local programs, and work toward a more comprehensive, standardized approach)
  - Indonesia, Malaysia, Phillipines, Singapore

Canada

- Historically has stated that elements of its drug review program were sufficient to address needs of those with rare diseases
- Continued push back from rare disease community has resulted in reconsideration of that view
- Currently working on development of a program for rare diseases

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Elements of Orphan Drug Programs

- Requirements
  - All programs have a prevalence criterion, varies
  - Some have additional clinical criteria
- Incentives include:
  - Market exclusivity
  - Priority review
  - Decreased/waived fees
  - Grants or tax credits
  - Protocol assistance/scientific advice
  - Waiver of local clinical trial requirements

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Need for a Variety of Incentives

- Sometimes the benefits of programs are not practically a benefit
  - Market Exclusivity may not constitute a true benefit if the other exclusivities (patent, data exclusivity) are of the same length
- Reduction of scientific advice fees, if advice not needed
- Slightly better price reimbursement, if separate application is needed for the orphan indication (may require partial application fee and costs for maintaining the application)

Some Issues Related to Orphan Drug Programs

- For second indication need a separate trade name and marketing authorization for EMA
  - Administrative challenges of having two or more marketing application authorizations
- May need for trials to be run on Asian subjects
  - Takes more time to conduct the studies if not one during initial development, so may have delay in access for patients (sometimes requirement is waived)

What does this mean for rare disease drug development?

- Increased understanding of the opportunities and challenges of rare disease development in countries throughout the world
- Development of new programs by Health Authorities throughout the world provides opportunities to shape those programs
- Advocate for appropriate programs and incentives, both when initially being developed, and afterward

Examples of Industry Advocacy Opportunities

- Trade Associations (e.g., US BIO (Biotechnology Industry Association, PhRMA, EFPIA)
  - BIO has a new committee for Orphan Drugs
- TREAT Act – legislation being developed to add flexibility to accelerated approval pathway, use for rare diseases
- Comment directly on Health Authority documents
  - FDA Orphan Drug Proposed Rule, issued in fall 2011
- User Fee Act Renewal – Improvements negotiated
  - Increased meetings and advice during development and review process
    - Includes new program for communications with FDA when sponsors have difficulty getting responses from reviewers

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Thank you for your attention.

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