Patient-Focused Drug Development Public Meeting

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October 25, 2012

Patient-Focused Drug Development

- Assessment of a drug's benefits and risks involves analysis of the severity of condition and current state of treatment armamentarium
- Patients who live with a disease have a direct stake in drug review process and are in a unique position to provide input on:
  - Analysis of severity of disease condition
  - Current treatment options
- Review process would benefit from systematic approach to obtaining patient perspective on disease severity or unmet medical need

FDA Approach to Drug Benefit Risk Assessment is Organized Around 5 Key Considerations

- Analysis of Condition
- Current Treatment Options

→ Provides regulators with the clinical context for weighing benefits and risks

- Benefit
- Risk
- Risk Management

→ Incorporates expert judgments based on evaluation of the efficacy and safety data and the expected impact of efforts to reduce and further characterize risks

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Analysis of Condition

From patients' perspective:

- What are clinical manifestations of the disease have the greatest impact on patients?
- Are there other aspects of the disease that have a significant impact on a patient's daily life? (e.g., impaired mobility, sleep problems, etc.)
- How do the clinical manifestations change with disease progression?
- How do the other aspects of the disease change with disease progression?

Current Treatment Options

From patients' perspective:

- What is the current standard of care?
- What therapies are being used to treat the condition (including approved and indicated therapies, drugs used off-label, and non-pharmacological therapies)
  - How effective are the existing therapies at treating the clinical manifestations of the disease?
  - How well do they mitigate other aspects of the disease?
  - How well tolerated are the existing therapies?
  - How does the effectiveness of approved therapies change with progression of the disease?
  - Does therapy effectiveness vary by patient sub-population?

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Patient-Focused Drug Development under Prescription Drug User Fee Act (PDUFA V)

FDA is undertaking a systematic effort in PDUFA V:

- PDUFA V provides resources to support additional program staff to expand activities dedicated to providing review divisions with patient input
- FDA will convene meetings with participation from review divisions, the relevant patient advocacy community, and other interested parties
- FDA will hold four public workshops each year over the next 5 years
  - Each meeting will focus on a different disease area, reviewing the armamentarium for that indication, and identifying areas of unmet need

Launching this PDUFA V effort

- CDER and CBER developed a preliminary list of ~40 disease areas for potential meeting focus, and published list in the Federal Register http://www.gpo.gov/fdsys/pkg/FR-2012-09-24/pdf/2012-23454.pdf
- Identifying disease areas for PDUFA 2013-2017 effort
  - Will determine the set of disease areas for FY 2013-2015, then initiate another public process to determine the set for FY 2016-2017
- Goal of today's meeting:
  - Get public input on FDA's published preliminary list of nominated disease areas for the patient-focused drug development initiative and the criteria used for nomination
  - Public also has opportunity to provide comment through online docket

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Preliminary list of disease areas: Criteria FDA used

Nominated diseases from wide range of areas

- Chronic, symptomatic, and affect functioning and activities of daily living
- Important aspects of disease currently not formally captured in clinical trials
- Reflect a range of severity
- Severe impact on identifiable sub-populations (e.g. children or elderly)
- Represent a broad range in terms of size of the affected population
- Currently no therapies or very few therapies, or the available therapies do not directly affects how a patients feels, functions, or survives

Preliminary disease area list

- Pulmonary arterial hypertension
- Heart failure
- Primary glomerular diseases
- Narcolepsy
- Huntington's Disease
- Depression
- Autism
- Peripheral neuropathy
- Fibromyalgia
- Obesity
- Nocturia
- Chronic fatigue syndrome
- Irritable bowel syndrome
- Inflammatory bowel disease
- Alopecia areata
- Diabetic ulcers
- Female sexual dysfunction
- Interstitial cystitis/painful bladder syndrome
- Fracture healing
- Diabetic foot infections
- Hepatitis C
- HIV
- Patients who have experienced an organ transplant
- Sickle cell disease
- Chronic graft versus host disease
- Amyloidosis
- Aplastic anemia
- Melanoma
- Lung cancer
- Cancer and young patients
- Cancer treatment in pregnancy
- Cancer and sexual dysfunction
- Cancer and depression
- Clotting disorders (e.g., hemophilia A (factor VIII deficiency) and von Willebrand disease)
- Thrombotic disorders (e.g., antithrombin deficiency and protein C deficiency)
- Primary humoral immune deficiencies (e.g., common variable immune deficiency)
- Neurologic disorders treated with immune globulins (e.g., chronic inflammatory demyelinating polyneuropathy)
- Hereditary angioedema
- Alpha-1 antitrypsin deficiency

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Some Key Objectives For Process

- Get broad patient input
  - Who can represent the views of patients?
  - Responsibilities of those who provide input?
- Use effective format(s) for collecting patient input
  - Faithfully capture patient views and represent transparently
  - Provide usable useful input to later FDA reviewer assessments
- Use venues/approaches that are both accessible and reliable
  - In-person
  - Electronic
- Process discussion http://www.gpo.gov/fdsys/pkg/FR-2012-09-24/pdf/2012-23453.pdf

Thank you!

Incorporating Patient Perspectives

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October 25, 2012

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Outline

- FDA's role in drug development
- FDASIA & PDUFA V
  - Major goals and initiatives
- Importance of patient's perspective in drug development
- Key points

Drug Development

- FDA oversight generally begins when testing therapeutic potential of an investigational drug in human subjects
- Investigational Phases
  - IND = investigational new drug
- Marketing application
  - NDA (drug) = new drug application
  - BLA (biological product) = biologics licensing application
  - Marketing applications submitted towards the end of clinical investigational phases
    - If approved, becomes a commercially available product
- Not typically directly under FDA oversight
  - Basic scientific research
  - Translational research (non-interventional)
  - Pre-clinical

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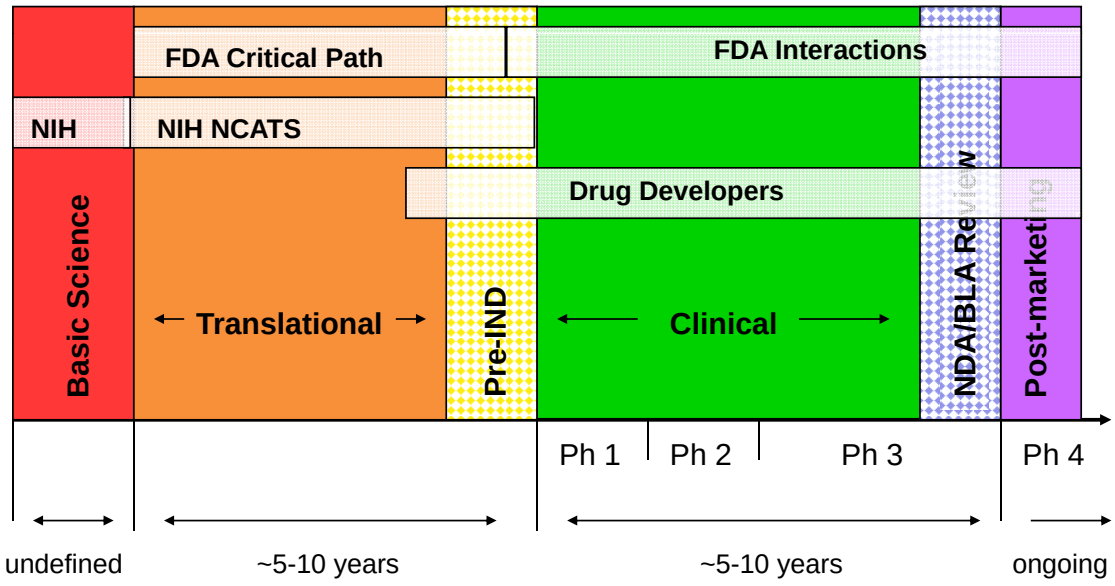
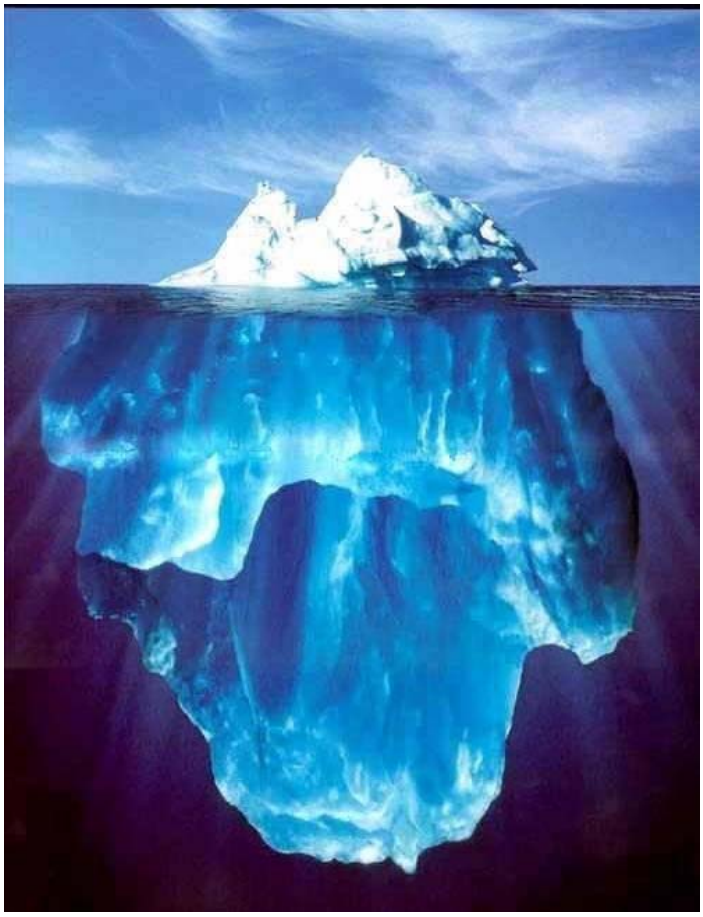
Overview of Drug Development



Drug Development (2)

- For marketing approval, drugs must be shown to be
  - Safe and effective for their intended use
    - Benefits outweigh the risks
    - Disease dependent – treatments for serious diseases often carry greater risks
  - Have “substantial evidence” of clinically meaningful benefit
    - Clinically meaningful interpreted as the impact of the intervention on how patients feel, function or survive



FDASIA & PDUFA V

- Major goals
  - Bring to market critical new medicines for patients
  - Maintain FDA's high standards for safety, efficacy and quality
  - Build on success of 20-year history of PDUFA
    - US leads the word in introducing innovative products to market[1,2]
  - Focus on regulatory science, benefit/risk framework, and patient-focused drug development
  - Several provisions to include perspectives of patients in the drug development process

[1]Roberts SA et al. Health Affairs. 2011;7:1375-1381

[2]Downing NS et al. N Engl J Med. 2012;366:2284-93

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FDASIA & PDUFA V (2)

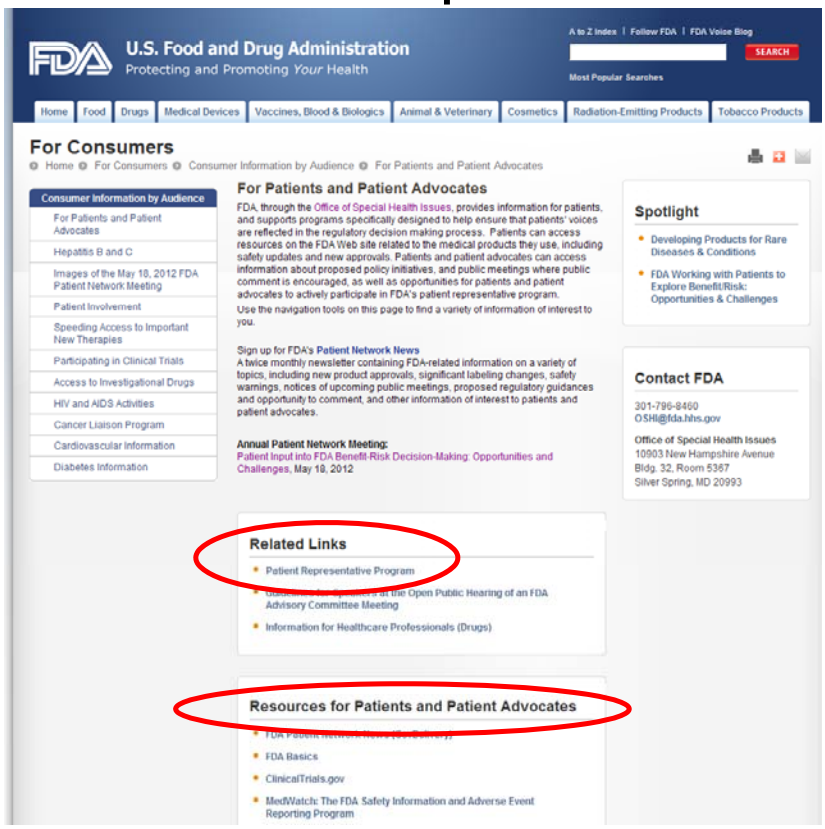
- Major initiatives
  - Disorders that are serious, life-threatening, life-limiting and/or have unmet medical needs, e.g.,
    - Breakthrough designation
    - Accelerated Approval
    - Rare diseases
    - Regulatory science development
  - Patient interactions, e.g.,
    - Patient focused drug development
    - Fostering participation in Patient Representative Program
    - Expert consultation

Patient-Focused Drug Development

- Also intended to inform development of:
  - Benefit-risk framework to facilitate decision making
  - Proposal to incorporate patients perspectives into Agency decision-making
- Broadly applicable to all marketing application review
  - Pilots
  - Emphasis on learning

PDUFA V Goals and Procedures, section X available at:
http://www.fda.gov/downloads/forindustry/userfees/prescriptiondruguserfee/ucm270412.pdf

Patient Representative Program



FDA Website
www.fda.gov

Office of Special Health Initiatives (OSHI)

For Consumers & Patients

http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/default.htm

Patient Representative Program (2)

The patient's perspective is important to medical decision-making. The patient representative program brings the patient voice to FDA advisory committee (AC) meetings (since 1991). Role is to provide the AC and FDA insight on issues pertinent to patients and family members living with a specific serious or life-threatening disease. Can be a voting or non-voting member of the AC.

Tiffany

Pompe Disease

Criteria:

Personal experience with the disease or condition

Articulate the perspective of patients

Experience as a patient advocate

Formal affiliation with a patient advocacy organization

Identify issues through communication with patient constituencies

Expert Consultation

- "EXPERT" (Sec 903)
  - "Consultation with External Experts on Rare Diseases"
    - For purpose of promoting the efficiency of and informing the review of new drugs for rare diseases
    - Encourages outside consultation with stakeholders on topics important to rare disease drug development
    - Experts are "individuals who possess scientific or medical training" on, for example:
      - Willingness and ability of individuals with a rare disease to participate in clinical trials
      - Assess benefits and risks of therapies
    - Consistent with existing authorities and protections under PDUFA V reauthorization and 18USC §202 (Special Government Employee) and 5USC §552(b) (Freedom of Information Act)

FDASIA available at: http://www.gpo.gov/fdsys/pkg/BILLS-112s3187enr/pdf/BILLS-112s3187enr.pdf

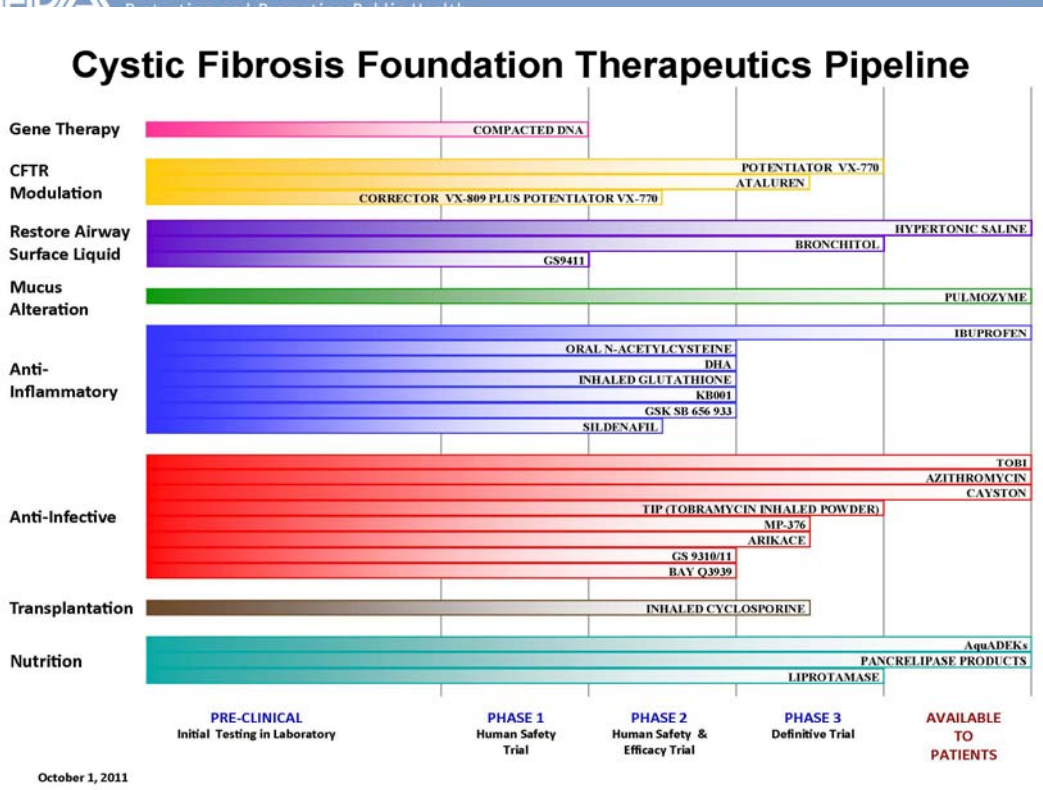
Key Point #1

- Numerous opportunities for involvement in drug development
  - Most value when involved early and throughout drug development process
  - Iterative process
    - Disease natural history
    - Endpoint and clinical outcome assessment (COA) development
    - Meaningful-ness of intervention and COA

Example: CF Foundation

- Historical information
  - Long-standing registry, disease well-described
    - CF registry and care network established in 1960
    - Extensive disease history prospectively collected which continues to inform research, development and patient care
  - 1980 - Research development program established
  - 1985- CF basic defect described
  - 1989- CF gene (CFTR) cloned
  - 1990's- CFTR biology advances rapidly
  - 2005- CFTR consortia funded as Manhattan-like projects to focus on CFTR trafficking, structure, and function

Slide courtesy of Preston W. Campbell, MD, CF Foundation.



Slide courtesy of Preston W. Campbell, MD, CF Foundation

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Key Point #2

- Communication, collaboration and transparency are key features of FDASIA, e.g.,
  - Increased outreach, such as
    - Public meetings
    - Workshops
    - Collaboration with FDA and other Governmental agencies, advocacy, industry, academia
  - Emphasis on learning from experience
    - Broader applicability to review process