FDA Draft Guidance Rare Diseases: Common Issues in Drug Development

An overview

Desmoid Tumor Research Workshop

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Outline

- Adequate description and understanding of the natural history of the disease
- Adequate understanding of the pathophysiology of the disease and the drug's proposed mechanism of action
- *Nonclinical pharmacotoxicology considerations*
- Reliable endpoints and outcome assessment
- Standard of evidence to establish safety and effectiveness
- *Drug manufacturing considerations*

Background

- Approval of all drugs is based upon demonstration of substantial evidence of effectiveness in treating or preventing the condition and evidence of safety for that use
  - One or more adequate and well-controlled studies

- Flexibility for rare diseases where there is a great unmet medical need
  - FDA “exercises its scientific judgment” in determining the kind and quantity of data a sponsor is required to provide for individual drug development programs

Natural History Studies

- Define the population (range, subtypes)
- Assist in study design
  - Duration
  - Subpopulations
  - Outcome measures
- Biomarker development

Pathophysiology/Biomarkers

- Estimating when to test the treatment in the course of the disease
- Estimate drug schedule to provide adequate exposure
- Identify therapeutic targets
- Biomarkers for proof of concept studies, dose and patient selection
- Identifying early markers and response to be used in adaptive and enrichment trial designs
- Assay development early in development program

Efficacy Endpoints

- Selection of appropriate endpoints is critical for trial to meet its objectives
  - Not well-characterized in many rare diseases
- Patient assessment tools
  - Understanding of disease including clinical characteristics of population under study
  - Understanding of which aspects of the disease are meaningful to patients
  - Assess suitability of existing tools and potential need to develop new tools or modify existing ones
  - Start early in development

Evidence of Effectiveness and Safety

- Require adequate and well-controlled trials
  - Clearly stated objectives
  - Valid controls for comparison
  - Well-defined patient populations
  - Minimization of bias in assignment and conduct
  - Well-defined and reliable assessments
  - Analyses adequate to assess effects of treatment
- No minimum number of patients
  - Persuasiveness of data, nature of benefit, safety, etc.

Rare Diseases: Common Issues in Drug Development

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Jonathan Goldsmith at 240-402-9959, or (CBER) Office of Communication, Outreach, and Development at 800-835-4709 or 240-402-8010.

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