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The Biosimilars Competition and Innovation Act: Overview and Life Cycle Planning for Biosimilars

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Impact of New Healthcare Policies on Biopharma Growth and Investment

- Healthcare reform law (Patient Protection and Affordable Care Act of 2010) will significantly affect biopharma growth and investment
- Focus on costs and cost-containment mechanisms
- A major element of PPACA is the Biologics Price Competition and Innovation Act

New Regulatory Approval Pathway for Biosimilars

- The Biologics Act in PPACA establishes a new regulatory approval pathway for biosimilars
  - Provides for approval of biological products as biosimilar or interchangeable (Section 351(k) applications)
    - i.e., expected to produce the same clinical effect and, if a multi-dose product, not present any greater safety or efficacy risk in switching from reference product
  - Provides that there be no "clinically meaningful differences" with the pioneer biologic product

New Regulatory Approval Pathway for Biosimilars

- FDA is granted substantial flexibility in determining approval standards for biosimilars, including whether and what type of clinical studies will be required and what differences in approval process from the BLA process are appropriate
- Grants 12 years of data exclusivity to pioneer manufacturers
  - 12 year exclusivity barring FDA approval of a 351(k) application determined from “the date on which the reference product was first licensed”
  - An application cannot be submitted to FDA until 4 years after the date on which the BLA for the reference product was first granted
    - Supplemental BLAs or slight modifications (undefined) are not included in the exclusivity period and do not extend it

New Regulatory Approval Pathway for Biosimilars

- Approval requirements are to be set by FDA, but should include, unless FDA waives them, the following:
  - Analytical studies demonstrating the biosimilar is highly similar to the reference product
  - Animal studies
  - A clinical study sufficient to demonstrate safety, purity, and potency
  - Other information showing that the biosimilar uses the same mechanism of action, route of administration, dosage form, and strength
- Exclusivity periods are provided for the first approved biosimilar commercially marketed
- Patent challenge provisions are significantly different from those under Hatch-Waxman for generic drugs, requiring “negotiation” of patent disputes and exchanges of patent information prior to instituting patent litigation

New Regulatory Approval Pathway for Biosimilars

- REMS requirements are mandated to apply to biosimilars as they do to the reference pioneer biologic
- Reimbursement for biosimilars is set at average sales price (ASP) plus 6% of the amount determined for the reference pioneer biologic
- Allows for imposition of user fees to review biosimilars
  - FDA has requested comments on options for a user fee program, 76 Fed.Reg. 27062 (May 10, 2011)

Issues Regarding New Regulatory Approval Pathway

- What is a biosimilar, and how similar to the reference product must a biosimilar be, to be approved and considered interchangeable
- What scope of data is necessary, if any, to show biosimilarity
- The scope of innovator modifications to a product that can provide a basis for additional exclusivity
- How important the manufacturing process is to showing biosimilarity

Issues Regarding New Regulatory Approval Pathway

- Naming issues for biosimilars (proprietary/unique or generic)
  - Effect on drug safety reporting/recalls
  - Effect on reimbursement
- Whether a biosimilar needs to provide data in connection with all approved uses of the reference product
- Whether a biosimilar can be better than the reference product ("biobetters"); if so, in what way (safety/efficacy)

Practical Issues Regarding Biosimilars Development and Marketing

- Effect on reimbursement treatment of the pioneer biologic of approval of a biosimilar, and of biosimilars themselves
  - Absence of express treatment of biosimilars in the new Act under Medicare Part B, Medicare Drug Pricing Program, Medicaid, 340B program
  - Whether biosimilars will constitute "multi-source drugs"
- Significant uncertainty under the new provisions in view of the substantial discretion provided to FDA regarding details and standards for submissions and approvals of biosimilars, and regarding the competitive market effects
  - See Congressional Research Service, *FDA Regulation of Follow-On Biologics* (April 26, 2010), describing the scientific challenges for FDA in approving biosimilars

Practical Issues Regarding Life Cycle Management

- Likely substantially different competitive market dynamics for biosimilars from that of generic drugs
  - See Federal Trade Commission, *Emerging Health Care Issues: Follow-on Biologic Drug Competition* (June 10, 2009), providing an analysis of the likely nature of competition in a biosimilars market and the significant differences likely compared with the competitive dynamics of the generic drugs market
    - Likely smaller numbers of entrants
    - Significantly greater cost of applications/testing
    - Likely less reduction in price from that of pioneer biologic
    - Necessity of marketing staffing for biosimilars, unlike generic drugs

Practical Issues Regarding Life Cycle Management

- What type and scope of sales/marketing approach and staffing
- What potential for use of authorized biologic settlement agreements, deriving from patent negotiation process
  - Continued controversy regarding drug patent litigation settlements ("pay for delay" settlements)
  - See Federal Trade Commission Report, *Authorized Generic Drugs: Short-Term Effects and Long-Term Impact* (August 2011)

Practical Issues Regarding Life Cycle Management

- What degree of cost reduction/difference with pioneer biologic will be needed to drive purchasing
  - Potential purchaser/payor concerns regarding interchangeability and safety/efficacy (potency)
  - E.g., Sandoz experience with purchaser resistance to Omnitrope (biosimilar somatropin) notwithstanding price advantage (Pink Sheet, Nov. 22, 2010)
- Potential for a biologics "evergreening" strategy
  - Use of pioneer biologics modifications to extend exclusivity period

Practical Issues Regarding Life Cycle Management

- Will payors require additional data regarding efficacy or safety for certain products, e.g., biosimilar monoclonal antibodies
- Will cooperation between the FDA and the European Medicines Agency (EMA) result in more expeditious approval of biosimilars in both jurisdictions
  - See EMA-FDA Report, Interactions between the European Medicines Agency and U.S. Food and Drug Administration, Sept. 2009 – Sept. 2010 (June 2011)
- FDA officials have noted that the Agency has conducted 14 pre-IND meetings for proposed biosimilar development programs, notwithstanding that the FDA has not yet issued proposed biosimilars regulations. (Pink Sheet, May 16, 2011)

Impact of Biologics Act on Biopharma Growth and Investment

- Biosimilars regulatory pathway significantly affects biopharma R&D, M&A, investment, and valuation of companies and products
  - Uncertainty of whether and when biosimilars will be approved
  - Uncertainty regarding sales and rate of return consequences of biosimilars on pioneer products
- Need to closely monitor and quickly adapt to regulatory and market changes in making biologic product investment and acquisition decisions

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