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New Government Healthcare Policies - Impact on Growth and Investment in the Biopharma Industry

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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

- Significant increase in population covered by health insurance (approx. 32 million) will result in substantial focus on cost-containment, including through administrative agency mechanisms

Impact of Healthcare Reform Law on Biopharma Growth and Investment

- Significant provisions affecting biopharma M&A, investment, and valuation of companies and products:
  - Comparative effectiveness research
  - New FDA regulatory approval pathway for biosimilars
  - Provisions affecting payors/healthcare providers as customers of product suppliers
    - Independent Payment Advisory Board
    - Quality of service/care guidelines
    - Accountable Care Organizations (ACOs)

Comparative Effectiveness Research

- Healthcare reform law contains provisions supporting the development of comparative effectiveness research (CER) concerning healthcare products and services
- Section 6301 establishes the Patient-Centered Outcome Research Institute (PCORI) to assist in conducting CER and disseminating research findings
  - PCORI is to identify national priorities, establish a methodology committee, and establish a research project agenda
- PCORI is required to ensure that CER "findings not be construed as mandates for practice guidelines, coverage recommendations, payment, or policy recommendations"
  - Private payers can, however, use such findings as a basis for their product or service approval or reimbursement decisions
  - Wellpoint released standardized CER guidelines on May 19, 2010 for use in evaluating drug coverage. (Pharmaceutical Law & Industry Report, May 25, 2010)
- Potential for controversy – e.g., rejection of 2009 recommendations by U.S. Preventive Services Task Force to end routine mammograms for women in their forties

Comparative Effectiveness Research

- Healthcare reform law allows CMS to use CER results to make a determination concerning Medicare coverage if such use is (1) through an iterative and transparent process, and (2) a determination to deny coverage is not based solely on CER
  - Note that the Agency for Healthcare Research and Quality is considering use of "academic detailing" to disseminate CER to healthcare providers (Pink Sheet, April 26, 2010)
- Significant practical limitations on use of CER including absence of accepted protocols, lack of historical CER studies for comparison, and controversy as to interpretation of results
  - Comparative effectiveness data was available for only about half of new drugs approved by FDA over the past decade (J. of Am. Med. Ass'n, May 4, 2011)

Comparative Effectiveness Research

- Importance of adding comparative effectiveness and cost effectiveness evaluations to drugs/biologics R&D programs
  - Increasing importance of inclusion of economic considerations at clinical trials stage
  - e.g., first comparative effectiveness trial of two pioneer drugs by National Institutes of Health
    - Comparative NIH trial of two Genentech drugs (Lucentis - $2,000/dose and Avastin - $40/dose) -- results showed both equally effective at treating an eye disease (Pink Sheet, May 9, 2011)
  - Potential for impact on drugs/biologics access and reimbursement
    - Note study on Australian drug market by Tufts University Center for the Study of Drug Development, concluding that "comparative effective research severely restricts access to drugs not deemed cost-effective." (Life Sciences Law and Industry Report, July 16, 2010)

Comparative Effectiveness Research Potential Applications

- Monitor assessments by the U.K.'s National Institute for Healthcare and Clinical Excellence
  - e.g., NICE decision not to recommend use of Takeda's bone cancer drug Mepact, based on its cost-effectiveness criteria, even though it stated that the drug "might represent a potentially valuable new therapy." Scrip,at 25 (Oct. 15, 2010).
  - e.g., NICE preliminary decision not to cover use of three leukemia products, Sprycel, Tasigna, and Gleevec, on the basis of clinical effectiveness and cost concerns. (Wall Street Journal, May 5, 2011)

Comparative Effectiveness Research Potential Applications

- Monitor potential for parallel reviews by FDA and CMS
  - Request for comments on proposed pilot program by FDA and CMS to conduct overlapping FDA premarket reviews and CMS national coverage determinations for certain innovative products when sponsors agree. See 75 Fed. Reg. 57045 (Sept. 17, 2010)
  - The Agencies suggest, in their Notice, that the proposed parallel review process "could also create incentives for venture capitalists and companies to increase their investment in innovative products by reducing the time to return on investment for those products eligible for parallel review"

New Regulatory Approval Pathway for Biosimilars

- Healthcare reform law establishes a new regulatory approval pathway for biosimilars (Biologics Price Competition and Innovation Act)
  - 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
  - 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

New Regulatory Approval Pathway for Biosimilars

- 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
- 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

New Regulatory Approval Pathway for Biosimilars

- 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 "arbitration" of patent disputes
- 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 recently requested comments on options for a user fee program, 76 Fed.Reg. 27062 (May 10, 2011)

New Regulatory Approval Pathway for Biosimilars - What the New Law Does Not Define

- 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
- 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")
- Effect on reimbursement treatment of the pioneer biologic of approval of a biosimilar

New Regulatory Approval Pathway for Biosimilars

- 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
- 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 with the competitive dynamics of the generic drugs market
- FDA officials recently 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)

Provisions Affecting Payors/Healthcare Providers as Customers

- Healthcare reform law is also a major event for most payors and healthcare providers, affecting their ability to pay for drugs/biologics
- Potential impact on product purchases from development of value-based purchasing (VBP) programs and quality of care/service performance indicators
- Potential effects on product purchases from development of accountable care organizations (ACOs) and bundled payment mechanisms
  - CMS recently issued proposed rules establishing the Medicare Shared Savings Program and creating ACOs, 76 Fed. Reg. 19528 (April 1, 2011)

Medicare Provider Potential Payment Changes

- Independent Payment Advisory Board (IPAB)
  - Significant new 15-member IPAB that will present Congress with proposals to reduce costs and improve quality for entire Medicare program
  - May address both products and services
  - IPAB cannot make proposals to ration care, raise taxes or Part B premiums, or change Medicare benefit, eligibility, or cost-sharing standards
- Wellpoint recently announced it is changing its system to pay increases only to those hospitals that score high enough on a test based on 51 indicators of treatment quality. (Wall Street Journal, May 16, 2011)

Consequences of New Government Healthcare Policies for Biopharma Growth and Investment

- Healthcare reform law presents significant challenges for biopharma M&A investment, and valuation of products or companies
  - Potential for restrictions on Medicare or Medicaid coverage and reimbursement from comparative effectiveness research
  - Potential for adoption of similar restrictions on coverage and reimbursement by private payors
  - Potential for approval of biosimilars of a biotechnology company's products
  - Potential for adverse impacts on product suppliers from value-based purchasing, use of quality of care guidelines and tests, and other payment restrictions imposed on payors and providers by the healthcare reform law or by private payors
- Need to closely monitor and quickly adapt to regulatory and market changes in making investment and acquisition decisions

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