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Preparing for a Biotechnology M&A – Corporate and Regulatory Insight to Keep Ahead of the Competition

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BioWorld Audioconference

Impact of Healthcare Reform Law on Biotechnology M&A

- Healthcare Reform Law (Patient Protection and Affordable Care Act of 2010, as amended by the Health Care Education Reconciliation Act of 2010) will significantly affect biotechnology company M&A.

- 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 Regulatory Due Diligence for Biotechnology M&A

- Most traditional areas of life sciences transactions regulatory due diligence are affected by Healthcare Reform Law
- Need to incorporate in biotechnology M&A regulatory due diligence the significant impact on healthcare providers, *i.e.*, payors and customers of product manufacturers
- Consequent substantial effects on, and uncertainty regarding, appropriate valuation of target products or companies.

Impact of Healthcare Reform Law on Biotechnology M&A

- Significant provisions affecting biotechnology M&A and valuation:
  - Comparative effectiveness research
  - Coverage of costs for certain clinical trials
  - New regulatory approval pathway for biosimilars
  - Provisions affecting payors/healthcare providers as customers of product suppliers

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 Research

- Consider adding comparative effectiveness and cost effectiveness evaluations to drugs/biologics R&D program
  - 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 currently being conducted
    - Comparative trial of two Genentech drugs (Lucentis - $2,000/dose and Avastin - $40/dose)
  - Potential for impact on drugs/biologics access and reimbursement
    - Note new 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)
    - See, e.g., the symposium articles on comparative effectiveness research in Health Affairs (October 2010)

Comparative Effectiveness Research
Potential Applications

- Monitor assessments by the U.K.'s National Institute for Healthcare and Clinical Excellence
  - e.g., NICE recently denied use by the National Health Service of two leukemia products, Sprycel and Tasigna, on the basis of clinical effectiveness and cost concerns (Pink Sheet, Feb. 15, 2010)
  - 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).

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."

Healthcare Reform Law - Coverage of Clinical Trials Costs

- Coverage of costs for certain clinical trials
  - Prohibits health plans from denying coverage of certain routine patient costs associated with participation in "approved clinical trials"
  - Includes trials that are:
    - For the prevention, detection, or treatment of cancer or other life-threatening diseases or conditions, and
    - Federally funded *or* conducted pursuant to an investigational new drug application (IND) or exemption (e.g., for drug-device combination products)

New Regulatory Approval Pathway for Biosimilars

- Healthcare Reform Law establishes a new regulatory approval pathway for biosimilars
  - Provides for approval of biological products as biosimilar or interchangeable
    - 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 determined from "the date on which the reference product was first licensed"
  - An application cannot be submitted to FDA for 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
- 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

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

- What is biosimilar, or how similar to the reference product a biosimilar must be, to be approved or 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”)

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
  - 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's public hearing on Nov. 2-3, 2010, on implementing the new biosimilars pathway may provide insight on the Agency's approach to evaluation of interchangeability, exclusivity issues, and user fees. See 75 Fed. Reg. 61497 (Oct. 5, 2010)

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
  - *See* Congressional Research Service, *Medicare Provisions in the Patient Protection and Affordable Care Act (PPACA): Summary and Timeline* (June 30, 2010), for a review and summary.
- Potential impact on product purchases from development of value-based purchasing (VBP) programs and quality of service performance indicators
- Potential effects on product purchases from development of accountable care organizations (ACOs) and bundled payment mechanisms

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
  - PhRMA intends to attempt to limit IPAB's potential power to make cuts in Medicare. (Inside Health Policy Daily News, July 14, 2010).
  - American Hospital Association has announced its support of legislation to repeal the IPAB. (BNA Daily Health Report, Oct. 28, 2010).

Consequences of Healthcare Reform Law for Biotechnology M&A

- Healthcare Reform Law presents significant challenges for biotechnology M&A and valuation of products or companies
  - Potential for restrictions on Medicare or Medicaid coverage and reimbursement from comparative effectiveness research
  - Potential for adoption of mirror restrictions on coverage and reimbursement by private payers
  - Potential for approval of biosimilars of a biotechnology company's products
  - Potential for adverse impacts on product suppliers from value-based purchasing and other payment restrictions imposed on payors and providers by the Healthcare Reform Law
- Need to closely monitor FDA and CMS development of regulations and administrative application of Healthcare Reform Law as to potential effects on product or company M&A valuations
- Need to adapt regulatory and market changes to evolving M&A structures and approaches

Current M&A Market Trends

2011 will hopefully be no 2010 and 2010 was certainly no 2009 . . .

Transaction Preparedness

- Alignment of constituencies – Shareholders, management, partners etc.
- Recognition of burdensome transaction demands on internal resources (management distract and the need to do perform “day jobs”)
- Need to retain capable & experience outside team: bankers, counsel, accountants, etc.

Transaction Process – Stage I
Preliminary Discussions / Documentation

- Letter of Intent / Term Sheet
  - Primarily used in private company acquisitions due to disclosure concerns
- Confidentiality Agreements
- Exclusivity Agreements
  - Raises meaningful fiduciary issues (esp. for public companies)
- Standstill Agreements
  - Primarily in public company context

Transaction Process – Stage I
Preliminary Discussions / Documentation
Selected LOI Issues . . .

- Letter of Intent / Term Sheet
  - Outlines important terms
  - Allows parties to identify the “deal breakers” quickly
  - Usually include an exclusivity period and confidentiality provisions, and hiring prohibitions, along with principal deal terms
  - Although not binding as to deal terms, very hard to back away from concepts
  - Live with this document throughout the transaction
  - Can file HSR off an LOI

Transaction Process – Stage I
Preliminary Discussions / Documentation
Selected LOI Issues . . . (continued)

- Agreement Issues to cover in LOI
  - Price
  - Earnouts
  - Post-closing adjustments
  - Assumption of debt or not
  - Form of consideration
  - Escrow / Holdback
  - Principal terms of indemnity
  - Principal closing conditions

Transaction Process – Stage I
Preliminary Discussions / Documentation
Selected LOI Issues . . . (continued)

- LOI Pitfalls
  - Lack of deadline / termination provision
  - Risk of being prematurely bound – must specify that there are no binding obligations until definitive agreement is signed
  - Avoid agreement to agree
  - Failure to pay close attention to non-solicit / no-hire provisions

Transaction Process – Stage II
Due Diligence

- Diligence allows buyer the opportunity to test the transaction's value proposition
- Back-stop the target's disclosure schedules
- Identify integration issues

Transaction Process – Stage II
Due Diligence (continued)

- Plan Ahead
  - Importance of Pre-transaction Knowledge Management (e.g., contract / license administration; maintenance of IP documentation; corporate records; etc.)
  - Establishment of Information sharing for Transaction (e.g., electronic data room)

Transaction Process – Stage II
Due Diligence (continued)

- Typical diligence issues considered for licenses/contracts:
  - Term (Renewal / Evergreen Provisions)
  - Assignment / Change of Control / Notice Provisions
  - Warranties
  - Guaranties
  - Indemnities
  - Liability Caps
  - Negative covenants (noncompetes)

Transaction Process – Stage III
Definitive Documentation

- Key issues:
  - Parties
  - Consideration – amount / timing / form of payment
  - Structure (assets / stock / merger / etc.)
  - Risk Allocation: Reps/Warranties & Indemnifications
  - Consummation certainty
    - Conditionality
    - Commitment to achieve Closing
    - Timing (termination / walk-away rights)

Bridging the Valuation Gap: Earnouts

- What is an earnout?
  - contractual right (embedded in an acquisition agreement) to future payment based on post-closing events/performance
- Key Earnout Issues:
  - Payment timing
  - Triggering event(s)
    - » e.g., achievement of performance metrics (development milestone for development products or performance milestones for marketed products

Bridging the Valuation Gap: Earnouts (continued)

- Pricing / calculation of payment
- Operating commitments by Buyer
  - » e.g., development / commercialization diligence
- Other operating issues
  - » cost containment (overhead allocation); treatment of add-on acquisitions, etc.
- Management Control
- Acceleration / Vesting of Payment
  - » e.g., CIC of Acquiror; divestiture of acquired asset/ business; termination of employment arrangements, failure to comply with operating covenants, etc.

Bridging the Valuation Gap: Earnouts for Public Companies (CVRs)

- The Challenge in “bridging the value gap” with owner/sellers of Public Companies
- CVRs are contractual rights that are issued to target company shareholders as part of the bundle of consideration delivered at closing.
- The CVRs allow the holder to benefit, usually in the form of a cash payment, upon the occurrence of a future event.
- CVR’s allow M&A practitioners to deploy private company deal solutions to overcome disagreements or uncertainties about the value or performance of a target in the context of public company deals.

Bridging the Valuation Gap: CVRs (continued)

- CVR's have gained traction in Life Sciences M&A, by allowing the parties to bridge value gaps with regard to:
  - Product approvals
  - Milestone payments associated with successful commercialization
  - Patent suits

Bridging the Valuation Gap: CVRs (continued)

- CVR's take the form of either:

(A) separate security that is publicly traded and transferable, or

  – Very limited due to expense and administrative burden

(B) An unregistered, contractual right that is transferable in very limited circumstances, such as estate planning.

  – Series of no-action letters by the SEC lay out five distinct features of a CVR that are necessary if the parties do not intent to register the CVRs.

Bridging the Valuation Gap: Option Deals

- A structure to address valuation challenges associated with (i) development products or (ii) before a meaningful assessment can be made of the market for commercial products
- An Option Deal is a “hybrid” of sorts between a customary license / collaboration transaction and an M&A transaction

Option Deals (continued)

- Typical elements of an Option deal:
  - License of one or more products for a negotiated period of time
  - Development and/or commercialization diligence commitments by licensee
  - Establishment in the license of an option (often exercisable by either licensee or licensor) upon achievement of applicable milestones to cause the conveyance of the product (*i.e.*, an asset sale, in the case where licensor has other products that are not included in the deal) or potentially the equity ownership of licensor (*i.e.*, an equity sale, in the case of a single product licensor)

Option Deals (continued)

- Milestones triggering option:

  (A) Development Products – typically developmental hurdles are set at completion of Phase II, Phase IIB and/or Phase III clinical trials

  (B) Marketed Products – typically negotiated revenue targets often after some period of time following product launch (e.g., 18 months)

Option Deals (continued)

- Option pricing:

  (A) Development Products – typically priced with reference to comparable products sold at comparable stages

  (B) Marketed Products – typically a negotiated multiple of revenue

- Call option (exercisable by licensee) – may last in duration 12 – 36 months from time of initial milestone triggering event

Option Deals (continued)

- Put option (exercisable by licensee) – may last in duration 12 – 36 months from time of initial milestone triggering event
- Call Option (exercisable by licensee)
  - Typically priced in the same manner as the Licensee's Call Option
  - Timing of exercisability is negotiated
- Documentation is very complicated resulting in meaningful execution risk

Bridging the Valuation Gap: Product Carve-outs

- A structure to address disparate views (as between a Buyer and Seller) regarding the value of products or development programs that are a part of a larger Company sale transaction
- Can take a number of forms, including:

(A) Pre-closing spin-off / distribution

(B) Pre-closing asset sale (to third party or affiliated transferee)

(C) Post-closing collaboration / JV

Risk Allocation through Indemnification

- Generally not applicable to Public Company Targets
- Compliance issues and other assumptions underlying valuation are typically subject to detailed representations and warranties
- Specific “hot button” issues are also often subject to specific indemnities to address risk allocation
- Key Issues for negotiation include:
  - Survival of reps/warranties and indemnity obligations
  - Contractual monetary limitations on recovery: Caps / baskets / *de minimis* limitations

Indemnification (continued)

- More Key Indemnification Issues:
  - Knowledge & materiality
  - Nature of recourse
  - Mitigation obligations
  - Obligations to pursue Collateral sources for recovery (e.g., insurance, if available, pursuit of claims against others, etc.)
  - So-called “Anti-Sandbagging” limitations

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