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BioPharma Collaborative Agreements: Choosing The Right Deal Structure

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Fierce competition in the pharmaceutical industry has changed the deal game. As always, companies are racing for the title of first to market with new products, first to achieve maximum market penetration, and the first to create barriers to competition. However, declining R&D productivity, rising costs of commercialization, increasing payor influence, shorter exclusivity periods, patent expiration on key products, a demanding regulatory environment, rising generic exposure, and an inability to compete across the entire drug development lifecycle has created an industry-wide pipeline crunch. The industry initially reacted to these factors by cost-cutting and frenzied merger activities. These activities, however, resulted in reducing the number of new drugs to market as companies dropped viable lead candidate programs.

Drug development is arduous, with an average development time of 10-15 years, of which 7 years represent clinical trials (www.innovation.org), and expensive and uncertain, with average costs of \$802-980 million for pharmaceutical drug development (with 75% of cost due to failures) and \$1-2 billion to bring a biotech product to market. *Ibid.* Of 5,000-10,000 compounds tested, 250 make it to animal testing, 5 to human clinical trials, and 1 is approved by the FDA. Moreover, only 1 in 3 approved drugs brings in enough revenue to recoup its cost of development.

The pipeline crunch resulted in a dramatic upswing in strategic collaborations: pharmaceutical companies recognized that these deals effectively leverage capabilities, cost-sharing, and a long term competitive solution. Likewise, strategic collaboration presented the perfect opportunity for the biotech company, often cash-strapped after initial funding, unable to handle the costs of clinical trials and regulatory approval, as well as the catastrophic liability from drug development. The number of new biotech-pharma deals has increased dramatically, from fewer than 400 deals in 1997, to double that number in 2007. (www.recap.com). Increased strategic collaboration is consistent with the acceptance of biology products and processes as primary research tools. Typically, collaboration comprises large pharma and biotech or specialty pharma. However, bio-bio

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and pharma-pharma deals are not atypical.

Early collaborations were reminiscent of the era of the robust pharma pipeline in which biotech contributed R&D and pharma committed the resources for clinical trials, regulatory approval and commercialization. Deal structure ran the gamut of pure patent licensing from biotech to pharma (no collaboration) to more collaborative deals such as co-commercialization, co-development, joint ventures and equity acquisitions. Co-commercialization deals included co-promote (the sale and marketing of a product under a single trademark, with cooperation in commercializing) and co-marketing (independent simultaneous sale and marketing by parties of a defined product under different trademarks) arrangements. The co-development deal combined discovery research and/or product development activities, with a continuing role by each party. The joint venture created a new entity to develop and market a drug. And the equity purchase in a biotech partner by a pharma partner represented the ultimate collaboration in terms of shared goals.

Collaborations between biotech and pharma were often limited to the patent license or the equity acquisition. The more collaborative relationships, such as co-commercialization collaborations, involved late stage products at or near commercialization and pharmaceutical partners with parity. Deals were struck in order to leverage the strength of the other party. For example, one pharma partner might enter into a co-commercialization arrangement in order to gain access to the other partner's strength in a particular market, by territory (e.g., strong ex-U.S. sales force) or field of use (e.g., BMS' reputation as a leader in oncology). Co-development deals tended to involved partners with less equal footing and late stage products. Naturally, the closer the product to launch, the more even the deal terms between the parties. Very few biotechs were of sufficient maturity to enter into co-commercialization or

co-development deals with pharma.

Deals for earlier stage products were more of a licensor-licensee arrangement with certain aspects of discovery research relegated to biotech; trials, regulatory and commercialization were left to pharma. In these deals, upfronts, milestones and dollars allotted to R&D were minimal, and pharma enjoyed the majority of downstream profits. Joint ventures were similar: biotech contributed intellectual property and know-how, pharma contributed cash and sales and marketing power with profits generated by the joint venture were slanted towards the pharma partner. Pharma, as the party undertaking most of the risk associated with these deals, was able to extract favorable deal terms.

Times have changed. As biotech has matured into the primary R&D source, and pharma's pipeline has emptied, the balance of power has shifted towards monetizing value early in the development lifecycle, either through lucrative early stage deals (consider the increased value of early stage deals from \$22 million in 2002 to \$85 million in 2006 (www.recap.com)) or M&A (e.g., Merck's acquisition of Sirna, Astra Zeneca's purchase of CAT). Indeed, the number of preclinical/phase I deals with large signing fees has increased significantly in recent years (In Vivo: The Business and Medicine Report, October 2006; www.recap.com). Moreover, in the quest to become full-service, biotech is now outlicensing to biotech with far more frequency. As part of the same phenomenon, co-promotion is becoming much more common at all stages of the product development lifecycle. *Ibid.* These data indicate that increased early stage deal drivers include the "buzz" surrounding a given technology, decreased perception of risk in early stage technology, and the need for pharma to defend its franchise.

Moreover, the recent decision of the United States Supreme Court in *KSR International Co. v. Teleflex Inc.* (550 U.S. ___ 2007), holding that a patent covering a new electronic gas pedal design was invalid because it was "obvious" in view of prior activity and knowledge in the field has changed collaboration deal structures. *KSR* raises the specter that the intellectual property underlying a collaboration technology will become invalid. Much has been written about this decision and its apparent minimal impact on the biotech industry, both in obtaining and defending patents. And the United States Patent and Trademark Office recently issued a statement indicating that its practice would not change very much in light of the *KSR* decision. (See *3 Industrial Biotechnology*, No. 2, 2007). Nonetheless, deal terms have changed; particularly with early stage biotechnology deals. Notwithstanding the possibility that intellectual property con-

tributed by a biotech partner may become nullified during the course of the collaboration, biotech has sought and successfully extracted greater upfront payments even in the post-*KSR* world.

Thus, in early stage deals certain deal terms have shifted, with an overriding theme of equality between the parties. Site, timing and control over preclinical and clinical development obligations have taken greater importance as have development expenses, FTE rates and costs. Biotech is keeping greater IP rights as well as the right to seek financing from big pharma. Upfront and milestone payments have increased; likewise, profit sharing has moved closer to a 50-50 split. Co-promote rights are oftentimes shared and it is not uncommon for biotech to retain rights in certain territories and indications. Quids are becoming far more prevalent as well.

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Governance structure has taken on greater importance with shared decision making the norm. Joint development, management, regulatory committees are common. Biotech often seeks a governance structure that allows it to tap into pharma's infrastructure, as for example, regulatory, legal, commercial operations, manufacturing, clinical and medical affairs, and drug safety and pharmacovigilance. On the other hand, biotech may take on more collaboration responsibility, particularly where it seeks to compete across the industry lifecycle, as a fully integrated company. Indeed, as biotech takes on more oversight, termination provisions are far more equitable.

These are interesting times for the biopharma industry. Collaborative relationships have enhanced the success of the industry. Recent biopharma alliances exhibit an overall clinical approval success rate of 30.2 percent vs. 21.5 percent for traditional pharma firm pipelines. (November/December 2006 Tufts CSDD Impact Report, The Tufts Center for the Study of Drug Development <http://csdd.tufts.edu/NewsEvents/NewsArticle.asp?newsid=69> (11/9/2006)). As valuation of early stage deals increases, the industry may witness greater M&A activity, and eventually, a return to a more robust pharma pipeline. Only time will tell.

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