



**MARCH 2009**

**MEMBER BRIEFING**

**LIFE SCIENCES PRACTICE GROUP**

---

## **Understanding Life Science Partnership Structures**

**Krist Werling, Esquire  
Bart Walker, Esquire  
Jessica Smith, Esquire**  
McGuireWoods LLP  
Chicago, IL, and Charlotte, NC

Companies in every industry that have attempted to raise capital and make research and development (R&D) investments over the past twelve months have faced significant challenges. The pharmaceutical and biotechnology sectors are no exception. The Dow Jones U.S. Biotechnology Index was down 18% during 2008, the pharmaceutical index DRG.X lost 19% of its market value. The entire healthcare industry has been battered during this downturn; the medical supply index DJUSAM was down 35% in 2008; managed care companies are down nearly 60%.<sup>1</sup> While a significant wave of consolidation is coming (as evidenced by Pfizer's announced acquisition of Wyeth), the partnership options described in this article offer options for pharmaceutical and device companies in these challenging economic times.

Dramatic declines in the capital markets have been in part caused by, and accompanied by the credit crunch. This restriction in available capital has brought significant challenges to transactions in all industries, including healthcare and biotechnology. The Biotechnology Industry Organization, a prominent trade group, recently stated that 180 publicly traded biotech companies have less than one year of cash on hand.<sup>2</sup> Both venture capital firms and private equity funds have been unable to structure leveraged buyouts and

---

<sup>1</sup> Lawrence C. Strauss, *Health-Care Stocks for an Ailing Economy*, BARRON'S, Nov. 24, 2008.

<sup>2</sup> Ron Winslow, *Investor Prospects Look Grim*, WALL ST. J., Jan. 11, 2009.

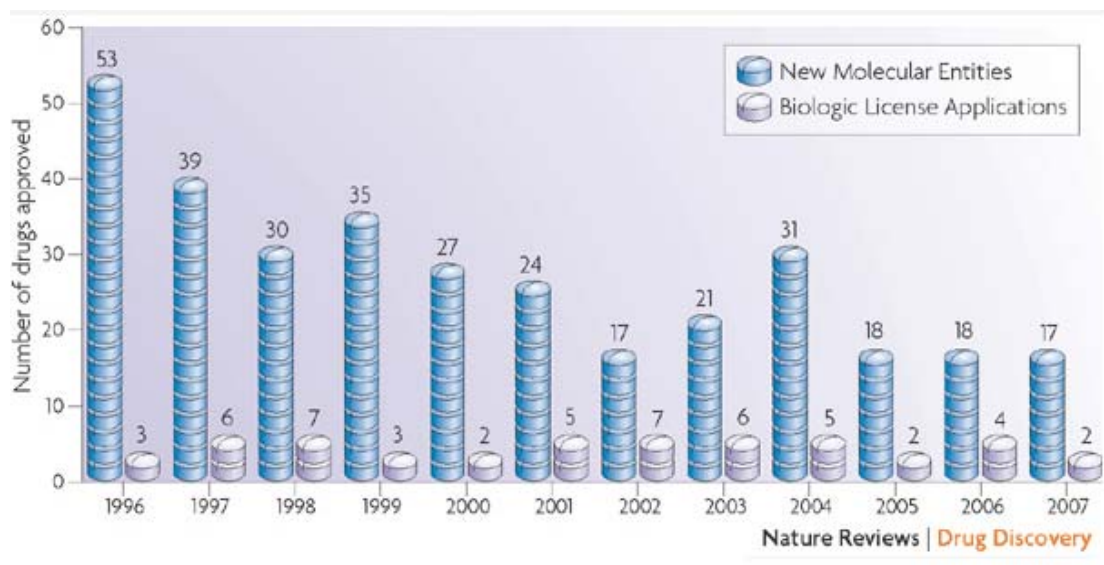
combination transactions requiring significant amounts of debt. As a result, a slowdown has occurred in the execution of both large- and middle-market-sized transactions. The lack of capital also has impacted the day-to-day operations for many life sciences firms, particularly those relying on capital from outside investors to advance R&D and bring new products to market.

Device and pharmaceutical companies also are facing non-economy-related pressures. Large, fully integrated pharmaceutical manufacturers are undergoing tremendous restructuring and cost-cutting efforts driven primarily by upcoming patent expirations and a lack of strong products in development pipelines. For example, in 2012 the following major drugs are scheduled to go off patent: Astra Zeneca's cholesterol drug Crestor; Forest Laboratories' antidepressant Lexapro; GlaxoSmithKline's diabetes drug Avandia; and Merck's asthma drug Singulair. Device and pharmaceutical companies also are confronted with a more conservative Food and Drug Administration (FDA) that is taking longer to approve new products and taking a more conservative approach to effectiveness review.<sup>3</sup> FDA continues to be scrutinized on its approval processes for medical devices, and approvals are expected to take longer because more clinical data is required.<sup>4</sup> Figure one shows the dramatic decline in the number of new drug and biologic approvals from 1996-2007. Throughout the industry, companies are looking for new ways to "extend the runway," as they race to bring new products to market before their cash reserves are depleted.

---

<sup>3</sup> Matthew Perrone, *FDA Approves More Drugs, Still Misses Deadlines*, WASH. POST, Dec. 19, 2008.

<sup>4</sup> See, e.g., GOVERNMENT ACCOUNTABILITY OFFICE REPORT TO CONGRESSIONAL ATTENDEES, *Medical Devices – FDA Should Take Steps to Ensure That High-Risk Device Types Are Approved through the Most Stringent Premarket Review Process*, Jan. 2009 ("We are recommending that FDA expeditiously take steps to issue regulations for each class III device type currently allowed to enter the market through the 510(k) process, including (1) reclassifying each device type into a lower class or requiring it to remain in class III and (2) for those device types remaining in class III, requiring approval for marketing through the PMA process.").



**Figure 1**

The result of these challenges has been a renewed focus in partnering efforts. For example, in 2008 63% of the year's top forty biotechnology transactions involved licensing or other types of partnering arrangements, rather than an outright acquisition of a target company.<sup>5</sup> Partnering can help life science firms deal with these twin challenges of a bear market and an increasingly conservative FDA. "Partnering efforts" is a general term used to describe the broad range of collaborations between life science companies. These strategies can provide needed capital or access to the skills necessary to bring products to market or keep research programs viable when outside capital is otherwise unavailable. Such efforts can include licensing arrangements, co-development, co-marketing, joint ventures, and a variety of other structures. The level of integration required to implement each varies from low to high, as does the technology development stage at which a given strategy is best implemented.

This article describes a variety of traditional life science partnering strategies, the unique advantages and disadvantages of each, and recent changes in partnering driven by the current economic environment.

<sup>5</sup> *Biotech Dominates 2008 Dealmaking – 150 Deals Announced Worth \$93.7 Billion*, The Dealmakers Forum, Levin and Associates, Jan. 28, 2009.

## **Strategic Investment**

A strategic investment involves one company making an equity investment or preferred debt investment in another company. This equity or debt infusion enables the recipient to fund future R & D efforts. This partnering strategy typically includes additional rights for the investor in either a specific product or category of products being developed by the recipient company. This may include, for example, preferential treatment in future investment rounds or a right of first refusal to acquire or license technology.

This partnering strategy has several advantages. It is a hands-off transaction that is simple to document and can be accomplished relatively quickly. Strategic investments typically involve very low integration between the investor and recipient. This effort may involve appointment by the investor company of one or more members to the recipient company's board of directors, but there is rarely a joint project team or other day-to-day input on the development of the recipient company's new products. The lack of integration and control also is the most significant disadvantage for the investing company—the investor has little real control over the direction of the R&D or the company itself.

Many large pharmaceutical companies and device manufacturers have their own venture capital arms to facilitate strategic investments. For example, Astellas Venture Management LLC (the corporate venture capital arm of Astellas Pharma Inc.) is dedicated solely to identifying biotechnology start-up companies with promising early-stage products. Astellas Venture Management's investment portfolio includes over twenty early-stage companies, including AkaRx Inc., CoMentis Inc., and Renovar Incorporated. Amgen, Eli Lilly, Johnson and Johnson, Pfizer, and Takeda have similar venture capital arms.<sup>6</sup>

## **Co-Development**

A second type of partnership effort can be characterized as a co-development relationship. A co-development relationship typically involves the joint

---

<sup>6</sup> George S. Mack, *Big Pharma Wants You*, BIOENTREPRENEUR, Sept. 22, 2006.

contribution of labor, intellectual property, capital, and other assets. Many large, fully-integrated pharmaceutical manufacturers and large device manufacturers have established teams that specifically identify and nurture co-development relationships. A co-development relationship is formalized when the parties enter into a Co-Development Agreement. The Co-Development Agreement typically establishes a joint project team that includes personnel from both companies who will oversee and contribute to the development of a product or category of products. A key component of the relationship is the provision of additional capital in the form of an up-front payment, with a number of subsequent milestone payments to move the project forward and toward product approval. Co-development agreements also may involve equity investment or preferred debt placement made concurrent with execution of the co-development agreement. Companies with later-stage technology to contribute typically have the most to gain from co-development relationships.

Co-development relationships are advantageous for the more-established party because they allow phased contributions and access to new technologies to add to existing product lines or bolster pipelines. Further, their collaborative team-oriented nature can create synergies and efficiencies for companies that have existing expertise in a therapeutic area. For companies possessing a technology that needs additional resources to bring to market, co-development relationships can offer access to capital and expertise to complete late-stage clinical trials or other late-stage hurdles.

There are two primary downsides to entering this type of relationship. A Co-Development Agreement does not result in the creation of a separate legal entity; therefore, both companies may bear liability resulting from the relationship. Consequently, insurance indemnification and other risk-allocation obligations should be structured carefully. Second, if the pairing does result in a successful product, profit and intellectual property may be co-mingled between the co-developers. This can result in difficulty when untangling the various assets, including intellectual property. Another key challenge is confidentiality and proprietary information. Entering into such a relationship may make secrets

harder to guard, and can give away certain valuable process information and trade secrets to competitors. In this regard, co-development relationships hedge risk, but also hedge reward.

GlaxoSmithKline (GSK) and OncoMed Pharmaceuticals entered in a co-development relationship in late 2007. The goal of this alliance was to discover, develop, and market new therapies that target cancer stem cells. Structurally, the alliance is being run through GSK's Center of Excellence for External Drug Discovery (CEEDD). One of GSK's goals for CEEDD is for it to help feed the GSK drug pipeline. OncoMed received an initial payment, the possibility of milestone payments, and future royalties. The agreement provides GSK with the option to license four of OncoMed's products. A key advantage for OncoMed here was the ability to leverage GSK's clinical development and commercialization capabilities.

Another recent example of co-development is the agreement Wyeth Pharmaceuticals and Santaris Pharma entered into in January 2009. Wyeth will give Santaris a \$7 million payment and invest \$10 million into the company.<sup>7</sup> The companies will use Santaris' locked nucleic acid drug platform to develop drugs with improved tissue uptake and half-life, and a higher resistance to metabolism. Santaris will be eligible to receive milestone payments for each of ten potential targets with the potential to total \$83 million dollars.

### **Joint Venture**

A third general category of partnering effort is the joint venture. A joint venture can involve any number of parties but in this arena most commonly involves either: (i) a larger pharmaceutical or device player and a start-up or (ii) similarly sized companies that have complementary technologies. The parties form a new entity—typically a limited liability company—to which each party will contribute some combination of assets, intellectual property, and personnel. The joint venture then takes responsibility for ownership and development of a product or category of products using the assets that have been contributed by both parties.

---

<sup>7</sup> *Wyeth, Santaris Reach Drug Development Agreement*, THE ASSOCIATED PRESS, Jan. 12, 2009.

Joint ventures require high integration, but the structure of the joint venture entity itself can be flexible and can be designed to meet the goals mutually agreed upon by the parties. Perhaps the largest benefit of a joint venture as compared with other bio-partnering arrangements is that the separate entity structure generally limits the liability of each individual party to its contribution to the joint venture entity. This separate entity structure of a joint venture affiliation does bring some challenges, however. A joint venture can be difficult to unwind. Further, governance issues may arise: there are only two ways to structure voting rights in a two-party joint venture: voting is either split evenly between the parties—which can lead to deadlock—or one party holds a majority of the votes—which can leave the minority party with less control over the venture. Finally, joint venture collaborations between certain parties may raise antitrust concerns. The Federal Trade Commission (FTC) has released “Collaboration Guidelines” to assist parties in structuring compliant joint ventures.

Medtronic Inc. and Genzyme formed a new joint venture entity in 2004 called MG Biotherapeutics LLC. MG Biotherapeutics will use cell-therapy research contributed by Genzyme and delivery system technology developed by Medtronic to develop novel treatments for advance cardiovascular disease. The venture started with fifty employees in three locations.<sup>8</sup> The board is currently composed of Medtronic and Genzyme executives.

A more recent example of joint venture partnering is the biosimilar generics joint venture entered into by Teva Pharmaceutical Industries and Lonza Group in January 2009. Teva and Lonza formed the joint venture to develop generic off-patent biological drugs. Teva’s primary contribution will be its low-cost manufacturing expertise. Lonza will contribute its ability to successfully build complex biotech drug manufacturing plants and subsequently produce such drugs under contract. Teva and Lonza plan to split costs and revenues evenly.<sup>9</sup>

---

<sup>8</sup> *Medtronic and Genzyme Form Joint Venture*, N.Y. TIMES, June 2, 2004.

<sup>9</sup> Andrew Kacj and Haig Simonian, *Teva and Lonza Form Generics Joint Venture*, FINANCIAL TIMES, Jan. 20, 2009.

The joint venture's plan is to produce most of the top ten biological drugs coming off patent over the next decade.

### **License Agreement**

A traditional license agreement is the fourth type of partnering effort that device and pharmaceutical companies may consider. Licensing can occur at nearly any stage of product development and typically involves up-front payments to a product developer by an entity who will receive the exclusive right to use or market the technology. Up-front payments also are found in the co-development partnering strategy discussed earlier. Licensing differs from co-development in that licensing generally involves less integration and collaboration between the partnering entities.

Entering into a licensing agreement is advantageous for the licensee because fees can be structured to fluctuate with sales success. Further, licensing a product typically costs the licensee less than developing a technology or buying it outright. The licensor benefits from such an arrangement when the licensor lacks resources such as capital or manpower to bring a product to market.

A few drawbacks to licensing exist. From a licensor's perspective, licensing a product diminishes profit potential. The licensor also loses total control of the product's form in the marketplace. Similarly, the licensing agreement may prohibit the licensee from altering the technology significantly to fit their needs or may prohibit uses in certain therapeutic areas. Licensing can also—similar to joint ventures—bring up unique antitrust concerns. The FTC may view an exclusive license as an acquisition of intellectual property, which would make the transaction reportable under the Hart Scott Rodino Act.<sup>10</sup> The FTC has released a guidance covering intellectual property licensing that can assist entities in structuring a compliant licensing agreement.<sup>11</sup>

---

<sup>10</sup> 15 U.S.C. §18a.

<sup>11</sup> *Antitrust Guidelines for the Licensing of Intellectual Property*, U.S. DEP'T OF JUSTICE and the FED. TRADE COMM'N, Apr. 6, 1995.

Pfizer Inc. obtained an exclusive license for Avant Immunotherapeutics' Phase 2 therapeutic cancer vaccine candidate CDX-110 on April 16, 2008. Pfizer made an initial payment of \$40 million to Avant and a \$10 million equity investment in the company. Under the agreement, Avant also will be eligible to receive milestone payments if Pfizer is able to successfully develop and commercialize CDX-110. The agreement was subject to FTC approval under the Hart Scott Rodino Act, and the parties obtained clearance less than one month after public announcement of the agreement.

### **Co-Marketing Arrangement**

Co-marketing a product is the final basic type of partnering effort. A co-marketing arrangement typically is entered into with a later-stage product. Royalty payments are exchanged for the right to produce and/or sell a product. This type of arrangement most commonly permits both parties to sell a product, sometimes in distinct market segments. Entering into a co-marketing arrangement is an effective method of increasing market penetration when financing for marketing efforts is limited.

The major drawback of this type of arrangement is that co-marketing can be viewed as anti-competitive behavior, particularly when parties share pricing and marketing information. However, the Department of Justice (DOJ) has approved a variety of co-marketing arrangements so it is possible to structure a co-marketing arrangement without engaging in prohibited anti-competitive behavior.

Olympus America Inc. and C.R. Bard Inc. entered into a co-marketing arrangement in 2001 to market and sell endoscopy products such as forceps. The arrangement designated Bard as the exclusive dealer for Olympus endoscopy accessory products. Olympus became a non-exclusive sales agent for Bard's products. This arrangement was submitted to and approved by DOJ. The two primary factors in the approval decision were that Olympus' products were reusable and Bard's were disposable, and that combined Bard and Olympus' share of these types of products did not significantly exceed the 20%

market share threshold that is commonly used in these types of analysis.<sup>12</sup> Key factors that go into an antitrust analysis of this type include market share under the arrangement, control of the collaboration's competitively significant decision-making, the likelihood that anti-competitive information will be shared between the parties, and any pro-competitive benefits that will result from the collaboration.<sup>13</sup>

### **Recent Changes in Partnership Strategies**

The current economic climate has left some potential partners with limited cash available to fund outside activities. For example, anticipating upcoming patent cliffs, many large, fully-integrated pharmaceutical manufacturers have adopted strategies intended to conserve cash. As a result, partnering efforts are evolving in the current economic environment.

Companies that have fared well during the downturn are seeking bargain-priced acquisition targets because of depressed values. For example, Abbott Laboratories, whose fourth quarter 2008 profit increased 28% largely due to its dual successes with Humira and the Xience heart stent, is "browsing small and medium-sized companies that make medical-technology products" because Abbott has \$3.77 billion cash-on-hand and "it's a good time to be a buyer."<sup>14</sup> Medtronic is another company that has fared relatively well in the downturn and is open to making small acquisitions "if the price was right."<sup>15</sup>

One recent exception to this is Pfizer's \$68 billion acquisition of Wyeth, announced in January 2009. This acquisition was driven primarily by Pfizer's upcoming patent expirations and its desire to diversify its healthcare portfolio. The acquisition price was necessarily a bargain, but Wyeth was uniquely positioned to help Pfizer diversify and fix its patent-expiration problem because of Wyeth's strength in targeting unmet biotechnology needs.

---

<sup>12</sup> Letter from Charles A. James to Philip S. Van Der Weele, DEP'T OF JUSTICE ANTITRUST DIV., Aug. 29, 2001.

<sup>13</sup> *Antitrust Guidelines for Collaborations Among Competitors*, FED. TRADE COMM'N and U.S. DEP'T OF JUSTICE, Apr. 2000.

<sup>14</sup> Tom Randall, *Abbott Chief Sees 'Good Time' to Shop for Deals*, Bloomberg.com, Jan. 21, 2009.

<sup>15</sup> Ben Hirschler, *Medtronic Sees 'Tuck-In' Buys, No Big Deals*, Reuters.com, Jan. 28, 2009.

For companies that have not fared as well, partnership efforts that require lower integration or less up-front cash commitment have become increasingly popular. Following are three key trends in partnership strategies:

#### *Technology Licensing to Raise Cash*

Technology licensing has increased in various niche areas. This is a result of development firms seeking to monetize assets through licensing technologies that are not central components of their research. Licensing these non-core assets can provide a necessary cash infusion to the developing company. For the licensee, a technology license offers access to a new technology without an otherwise-significant commitment.

#### *Technology Asset Sales*

Technology asset sales also are becoming more prevalent. Asset sales do not involve significant partnering, but are appealing for companies that are desperately low on cash. The lack of available bank financing also has resulted in increased use of seller notes and earn-outs. When seller notes or earn-outs are used, a seller in an asset sale retains some stake in the outcome of the development program after the cash-generating activity has occurred.

Inflazyme Pharmaceuticals Ltd. and Biolipox AB entered into an asset sale in late September 2007. Biolipox acquired the majority of Inflazyme's assets, including its research and development programs on PDE inhibitors and protein therapeutics.<sup>16</sup> In exchange, Inflazyme received an up-front cash payment and the possibility of future lump sum payments based on clinical milestones. Inflazyme also retained the possibility for royalty payments based on key technologies.

#### *Extended Milestones*

Finally, most partnership activities where cash is provided to one of the partners are being provided on a milestone-based structure. Even deals involving firms

---

<sup>16</sup> *Inflazyme Pharmaceuticals, Ltd. Signs Asset Sale Agreement with Biolipox AB for a Potential Value of up to \$11 Million, Plus a Royalty Payment*, BIOSPACE, Sept. 24, 2007.

with highly marketable technology are being faced with milestone structures instead of lump-sum strategic investments or co-development arrangements. Growth companies evaluating these possible arrangements should carefully plan achievable milestones that will coincide with capital needs. This will enable R&D efforts to survive through an unknown length of time during which the credit crunch will continue to make cash hard to come by.

## **Conclusion**

Pharmaceutical, biotechnology, and medical device companies currently face significant economic and non-economic challenges. Tumult in the capital markets and the resulting credit crunch have significantly restricted the amount of available capital. Approaching patent expiration deadlines also will impact device and pharmaceutical companies' bottom line. Further, the FDA has recently taken a more conservative approach to effectiveness review, and new drug and device approval times are increasing.

Partnering efforts are one viable strategy a pharmaceutical, medical device, or biotechnology company should evaluate during these challenging times. Entering into a licensing arrangement, co-development or co-marketing effort, or a joint venture can provide a company with needed capital and access to the skills necessary to bring products to market or keep research programs viable. Further, partnering can be an effective alternative to an IPO or selling an entity to a fully integrated pharmaceutical company or device manufacturer. The partnering strategies presented in this article are the most basic options in their fundamental forms. Various hybrids of each are possible and can be individually tailored to meet unique objectives.

***Understanding Life Science Partnership Structures*** © 2009 is published by the American Health Lawyers Association. All rights reserved. No part of this publication may be reproduced in any form except by prior written permission from the publisher. Printed in the United States of America.

Any views or advice offered in this publication are those of its authors and should not be construed as the position of the American Health Lawyers Association.

“This publication is designed to provide accurate and authoritative information in regard to the subject matter covered. It is provided with the understanding that the publisher is not engaged in rendering legal or other professional services. If legal advice or other expert assistance is required, the services of a competent professional person should be sought”—*from a declaration of the American Bar Association*