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Putting the "Co" in Development and Promotion

The New Biotech-Pharma Collaborations

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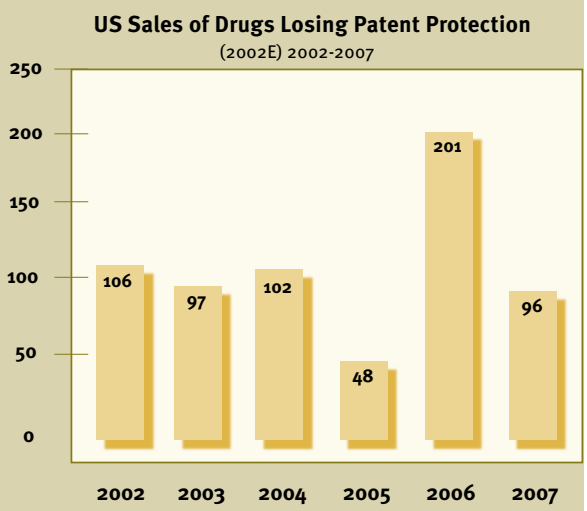
A number of strategic reasons exist for partnering among life sciences companies. For emerging biotech companies, partnerships and strategic alliances provide a number of benefits, including much needed capital infusions, sharing of risks for continued drug development, and access to pharma or biopharma clinical, regulatory or commercialization expertise.

While collaborations between emerging biotechnology companies and pharma/biopharma companies are not new, these deals dramatically have increased in sheer number and deal value. Perhaps the most important recent trend to note is a structural one—a trend away from the conventional royalty model toward 50/50 cost and profit sharing collaborations. Last year, even small, emerging biotech companies successfully negotiated balanced deals with 50/50 economics. In spite of the resource constraints small biotech companies face, and the inherent complexity in negotiating 50/50 collaborations, these partnering deals are on the rise.

EXHIBIT I



Understanding What's Driving Pharma

Two main factors are driving pharma's ongoing collaborative fervor. In today's market, pharma companies are experiencing falling productivity from their internal pipelines. Gaining access to new products through alliances with biotech companies allows pharma companies to expand their pipelines and increase their probability of success. Also, due to the complexity of manufacturing, biologics tend to have less competition than conventional synthetic chemical medicines, thus providing a more stable revenue stream.

Deal in Focus—Merck and Agensys

Cancer-focused Agensys licensed its Phase I prostate cancer drug to Merck for $17.5 million in upfront payments and up to $11.5 million over the next year in milestone payments. Merck and Agensys will co-develop and jointly fund the drug AGS-PSCA for advanced prostate cancer and other indications through Phase II. Merck will assume primary responsibility for commercialization, commercial manufacture and worldwide clinical development while Agensys will retain substantially equal participation rights in each of these areas. Agensys has an equal number of representatives on the development and commercialization committees, and has the right to co-promote in the U.S.

The Agensys deal provides several benefits to Merck – most notably, the opportunity to be involved with a promising cancer treatment drug at an early stage and the lower risk associated with funding an earlier stage drug through milestone payments. Meanwhile, Agensys retains equal control over development and commercialization of its drug and obtains needed development funding immediately.

Pharmaceutical companies increasingly are capitalizing on these benefits to drive significant revenue. Wyeth, for example, today relies on biotech product revenues to drive approximately 25% of its revenues. Within the next 5-10 years, Wyeth expects revenues generated from biotech products to grow to 40% of total revenues.

RISING DEVELOPMENT COSTS

Recent studies estimate that development and FDA approval of a single drug compound costs between $800 million and $1 billion. Additionally, the newly intense regulatory pressure to address safety concerns can add significant cost and resource requirements to bringing a drug to market. In this situation, it makes sense for a biotech company to consider a partnership or collaboration to help manage the cost and risks of further development.

Another compelling factor is that a significant number of blockbuster drugs are coming off patent. See Exhibit I. As a result, pharma companies—and increasingly large biotech companies—have expanded their hunt for products to in-license from smaller biotechs. This, in turn, creates significant leverage for emerging biotech companies. The October 2005 deal between Merck and Agensys is a clear illustration of this trend. See Deal in Focus—Merck and Agensys.

Understanding the Biotech Drivers

Biotech companies operate in an environment of significant financial constraints. One key obstacle is the ever -increasing amount of cash required to support continued drug development. Most emerging biotechnology companies do not have sufficient capital, research and development capabilities, regulatory expertise, commercial infrastructure or manufacturing capacity to fully develop and commercialize a product on their own. As a result, collaborative deals with pharma offer biotech access to critical resources to fill operational gaps—global sales capabilities, regulatory expertise, R&D depth and commercial and manufacturing infrastructure.

Co-Development and Co-Promotion Considerations

In the not-too-distant past, biotech product deals were fairly straightforward: the small biotech company with an innovative drug in early stage clinical development turned to a large pharmaceutical company to take over the future development and commercialization of the product. These deals generally were structured as exclusive licenses to the pharma partner, in return for an upfront fee, milestone payments and royalties on product sales.

While the prospect of sharing the costs of late-stage development through product commercialization can be a high-risk proposition for many small, financially-strapped biotechnology companies, 50/50 economic structures provide the smaller partner with an opportunity to retain some degree of control over development and to ultimately capture a larger piece of the upside of a successfully approved and launched product. As important, a 50/50 deal represents a significant statement that the partners have strategic synergies and a shared operating philosophy that will be deployed by both parties to drive successful product development and commercialization.

The deal flow in recent years demonstrates an increasing trend away from the royalty model toward 50/50 shared economics, with the smaller company actively participating in the project and retaining equal control over critical development decisions, including where clinical trials will be conducted, who will provide the clinical supply material, and who will take the lead in interacting with the regulatory agencies in the U.S., Europe and other major markets.

If a co-promotion arrangement (usually for the U.S. market) is added to the mix, then the deal becomes more complex, but also more exciting for the emerging biotechnology company. With a co-promotion agreement, the small biotech company can bargain for the right to participate in the marketing and promotion of its drug product in the largest pharmaceutical market in the world—the U.S. market.

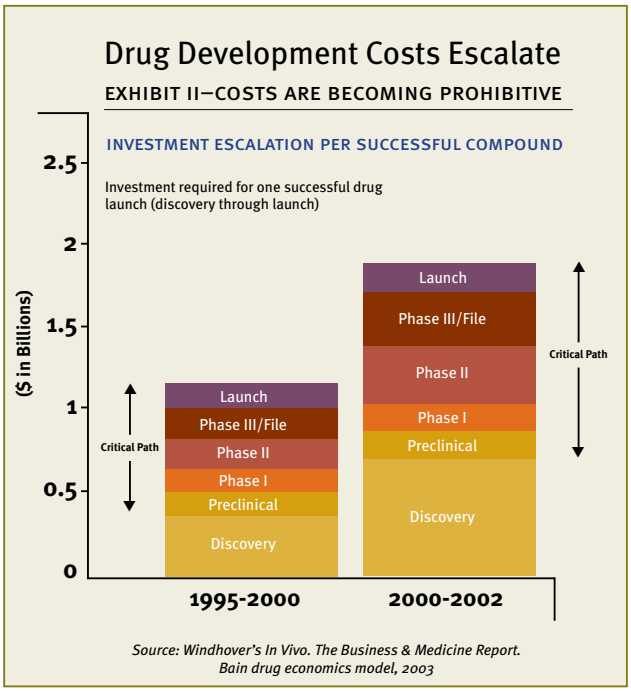
Fifty-fifty co-development arrangements or co-promotion deals represent attractive options for the smaller company that wants to control its product's destiny. However, these types of deal structures are much more complex than those based on the larger pharma partner taking full responsibility for development and commercialization. Consequently, these collaboration agreements require extensive planning and detailed negotiations.

Companies considering such a partnership or alliance with pharma or biopharma must consider a number of critical factors, including:

- Financial Modeling and Forecasting
- Control over Development
- Relationship between Partner Companies
- Planning for a Range of Outcomes

Financial Modeling and Forecasting

Can the smaller company afford a 50/50 cost sharing arrangement? This type of structure means not only sharing the product revenues but also the expenses, which can be considerable. See Exhibit II. Companies contemplating shared development cost arrangements must do their financial homework in the form of cost models, a risk adjusted net present value analysis and a detailed cash flow forecast. At each step of the analysis, be sure to identify the assumptions embedded in the financial forecasting. Remember that each assumption about the product's development path, launch time, and commercial market potential will be tested by the larger pharma partner during its due diligence.



As part of the analysis, companies should consider the size of the market opportunity, potential market share over time as well as development, marketing and other commercialization costs. Product pricing and payor/reimbursement issues should also be factored into the analysis. Finally, the analysis should incorporate realistic development, approval, launch, and peak sales time lines. Of course, the competitive environment, and its potential impact on these time lines, also should be included in the analysis.

The long-term nature of life sciences collaborations and strategic alliances makes these arrangements inherently unpredictable. It is important then to consider multiple scenarios when completing the financial analysis. The small biotech company should perform a sensitivity analysis varying the ramp up period, market share attainment, and cost scenarios. Biotech companies also need to carefully consider the timing of cash inflows and outflows because cash availability often is the most significant limiting factor.

In a co-promotion deal, negotiations will need to cover, among other things, financial issues such as allocation of promotional costs and expenses, number and quality of detailing, responsibility for sales force training, and monitoring and auditing of promotion expenses. Historically, biotech companies

have wanted to play a key role in promoting and marketing products to learn from the process and to build their own commercial infrastructure. But the key question that biotech companies should ask before making any decision is "Do we know what we're getting into?" It is easy to underestimate the cost and resource requirements associated with a co-promotion structure. Building a sales force and a marketing team, as well as building the brand for the product can cost a company millions of dollars—before any product sales revenue is even recorded.

The PDL BioPharma/Roche global asthma collaboration is an example of a biotech /pharma deal that included both a 50/50 shared ecomomic structure and a co-promotion arrangement. This deal amply illustrates the complexities that a biotech company must address to successfully negotiate and execute these deals.

PDL's relationship with Roche dates back to 1989, when it licensed to Roche worldwide rights to Zenapax, the first humanized monoclonal antibody approved by the FDA for the treatment of acute kidney transplant rejection. Over the years, PDL continued to conduct investigator-sponsored trials to test Zenapax' potential in autoimmune diseases and asthma. In 2003, PDL paid $80 million to Roche to buy back the rights to Zenapax, except for use in kidney transplant patients. Following the announcement of positive Phase II data in asthma, PDL approached Roche to negotiate a collaboration deal for Zenapax in asthma and other respiratory disorders. Key features in the asthma collaboration are equal representation and decision-making on development and commercialization decisions, a 50/50 cost-profit split, and a co-promotion arrangement in the U.S. Prior to agreeing to the collaboration with Roche, PDL committed substantial resources to the diligence process, with a focus, among other things, on: the potential product market share in asthma; the need to track sales in multiple indications, including transplant, asthma and multiple sclerosis; the development costs and risks, including the costs of developing a new high yield antibody manufacturing process; the estimated approval and launch dates; and, post-launch marketing and promotion costs.

Control over Development

In today's deal environment, biotech companies find that it is possible to obtain development funding from a larger partner without ceding control. An illustration is the 2005 deal between Theravance/Astellas. Astellas agreed to pay $65 million upfront and another $136 million in milestone payments based on clinical filings and approvals for the Theravance Phase III antibiotic Telavancin. Theravance successfully retained significant control over the clinical development and launch of Telavancin.

As with a co-promotion arrangement, successful negotiation of balanced development terms requires a good amount of strategic thinking and planning, along with detailed financial analysis. Some of the key considerations that must be assessed in a co-development deal include determining how and where clinical studies will be conducted and which party will assume oversight responsibility over the trials. Responsibility for development expenses and internal FTE rates and costs also must be discussed in detail, and agreed upon. A "meeting of the minds" on these key issues, generally through a negotiated development plan and budget, will solve a lot of potential problems down the road.

Relationship between Partner Companies

Whether a collaboration will be successful depends a great deal on the often unpredictable component of human capital. Therefore, it is important to consider the following before entering into a long-term collaboration:

- Management buy-in—Make sure that all major department heads are on board and have input into the deal parameters, e.g. finance, clinical, regulatory, and marketing divisions.
- Opportunity costs—Everyone—senior management, the board, the project managers—should understand that company capital and resources will be focused on the partnership and that these resources may not be available for other projects.
- Alignment of Interests—Both parties must be willing to negotiate and execute a deal that is based on long-term 50/50 economics. It is important to confirm with your partner that there is a shared operating philosophy going forward.
- Service levels and partnering support—Pharma companies typically have several products and therapeutic areas in their portfolio. Key questions here include: What is the pharma company's experience in the relevant therapeutic area? Will the pharma company champion the therapeutic and market potential of the product? Will the pharma partner give the product the level of attention and resources it will require?

Planning for a Range of Outcomes

As with any other key business decisions, various scenarios and strategies should be thoroughly evaluated. In particular, biotech companies should consider the potential downside of a 50/50 collaboration with pharma or biopharma. While sharing the risks and costs can be attractive, it comes at a price. Virtually any significant collaboration means that the smaller biotech company will give up certain rights in the drug candidate and in the related technology as well as relinquish significant management control. Sharing the "upside" can also be emotionally difficult for a company and its team when early sweat equity and risk-taking went into building the company and the product.

Finally, when considering any long-term partnering arrangement, companies need to have extensive internal discussions to address a number of key questions:

- Why is this proposed deal important for the company?
- Where do we want this deal to take us?
- What skill set do we expect our partner to bring to the table?
- Do we want this partner for the U.S. only? For the E.U.? For a global collaboration?
- If it is a global collaboration that is desired, should specific territories be carved out to facilitate licensing opportunities with other partners?
- How does the proposed deal fit within the company's short- and long-term goals?

Thorough advance preparation results in better deal-making and avoids unexpected surprises during the negotiation process.

Alternatives

When considering a 50/50 profit and cost share arrangement, or a co-promotion deal, a company should keep in mind alternative structures and scenarios, including the following, to maximize long-term flexibility:

- Retain co-promotion rights as an option, rather than a firm commitment.
- If concerned about having the cash available to fund 50% of the global development costs, consider building in the right to seek financing, on reasonable terms, from your partner.
- Consider an appropriate cap on the marketing budget, and mechanisms for annual "true-ups."

Conclusion

Partnering can be a win-win situation for both pharma and biotech. Pharma can increase its pipeline and manage its risk, while biotech may obtain much needed cash and developmental and commercial expertise. Pharma's desire to access earlier stage products provides leverage for biotech companies to negotiate more balanced partnering terms. Specifically, this leverage allows biotech to retain more control over the continued development, and ultimately, the commercialization phase, of the product, which has been a long-time goal. However, the 50/50 shared development structure deal is one that a biotech company needs to approach cautiously. Similarly, a co-promotion arrangement requires a significant amount of cash and resource attention—companies can easily underestimate what is required.

Partnering deal negotiations can be highly complex, extremely lengthy and resource intensive. Companies considering partnering arrangements must do financial and operational due diligence to ensure the success of the partnership, which includes creating a detailed financial model that incorporates variable scenarios, risk-adjusted net present value calculations and cash flow forecasts. The senior management team, as well as subject matter experts, should be consulted at critical points in the planning and negotiation process to assist in evaluating critical strategic questions and determining the best partnering approach. The key is to find the optimal path forward for continued development and, ultimately, commercialization of the company's drug compound—with a successful partnership as the means to achieve this end.

References

BIOWORLD Today, October 18, 2005; *Agensys, Merck Ink Potential $170M Cancer Antibody Deal*

Burrill & Company Report 2005

BIOWORLD Today, November 9, 2005; *Theravance Gets Telavancin Partner in Deal Worth $221M*

PRNewswire–FirstCall, September 30, 2005, *Roche and Protein Design Labs Restructure Commercial Alliance on Zenapax*

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