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STRATEGIC ALLIANCES PROPEL INDUSTRY PRODUCTIVITY

EXECUTIVE SUMMARY:

While mergers and acquisitions grab the headlines, a variety of strategic alliances — ranging from co-marketing, to joint ventures, minority equity alliances to consortiums — are a more common means for companies to leverage themselves in the marketplace. The results? Faster time to market and higher returns.

by Milton Liebman

Hardly a day goes by without the completion of a strategic alliance in the prescription drug industry. In fact, there were 674 pharmaceutical alliances announced in 1998, nearly three times the number of mergers and acquisitions that took place. Fifteen of these deals were valued at more than \$100 million. In 1999 the number of finalized pharmaceutical alliances was 602, as compiled by Windhover Information.

The pharmaceutical industry is under pressure to increase the number of major new drugs brought to market and it faces rising costs in doing so. U.S. companies invested \$20.1 billion in research in 1999, according to PhRMA. This year it is expected to

increase that amount by 11 percent. R&D as a percent of sales of research-based companies is growing annually. In 1999 it was 20.8 percent of sales. In 1990 it was 16.2 percent and in 1980 it was only 11.9 percent.

This investment requires payback, and strategic alliances are one way to expedite this. Use of alliances is growing as a means to help companies increase the number of new chemical entities (NCE) they develop, and speed the time needed to bring them to market. One study by Anderson Consulting reports that leading pharmaceutical companies plan to triple the number of NCEs brought to market this year and reduce the time need for approval from over nine years to 6.5 years by 2003.

Many of the present-day major blockbuster products were developed and marketed through research, development, licensing, and co-promotion alliances. We can expect more.

Erik Rule, partner at PricewaterhouseCooper predicts that this year "large pharmaceutical companies will dedicate as much as 30 percent of their R&D expenditures to external partnerships. It's a way of doing business." He defined an alliance as any situation where there is an explicit agreement to leverage combined resources to achieve competitive advantage.

There are basically four types of alliances. The advantages and formats of each were analyzed in the 1999 report 'High Performing Strategic Alliances' by Pricewaterhouse.

Strategic alliances

Cooperative partnerships are the most popular alliances. Rather than needing a separate enterprise, they take the form of virtual organizations, according to Rule.

These alliances tend to focus on individual projects such as co-marketing and product swaps, new technology for research improvement, or development of an NCE. They are relatively fast, easy, and economical — as long as structures and goals are defined at the outset, said the monograph.

It is clear that alliances can lead to mergers and acquisitions, as exemplified by the headline-creating Pfizer/Warner-Lambert relationship.

At a Pharmaceutical Strategic Alliance Conference in New York two years ago, Warner-Lambert's President of the Pharmaceutical Sector, Anthony H. Wild, Ph.D., detailed the origin of the Lipitor and Rezulin deals. Today as these companies merge, Lipitor will become an all-Pfizer product and Rezulin is off the market. But in 1997, successful strategic alliances were developed for these products with the idea of transforming the future of Parke-Davis, Wild said. The idea material-

ized, as both drugs became blockbusters. "Our relatively small size limited our commercial presence; our main competitors included some of the largest companies in the industry. How could we maximize the opportunities?" he asked. The answer was working with one or more partners.

A global launch of Lipitor was the biggest challenge. It would be the fifth statin introduced, going up against Zocor, Pravachol, Lescol, and Mevacor. In seeking

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a partner, Wild said, potential candidates were evaluated against several criteria, including cardiovascular expertise, absence of competitive issues, strong GP sales force capability, financial strength, global presence, track record of successful product launch, and record of successful collaboration with partners. Not much left out, but to this list was added "personal and organizational chemistry."

As the world knows, the answer was Pfizer. Wild explained that it was a long-term arrangement, with a seamless collabo-

ration on marketing, promotion, and sales. The deal was structured to provide incentives for success. The effectiveness of that structure became evident as one motivating factor in Pfizer's unwanted takeover bid for Warner-Lambert.

Concurrently, Warner took another strategic approach to co-promote Rezulin. It formed a joint venture with Sankyo. The deal gave Sankyo an early presence in the U.S. with an experienced partner. A full sales force was established through outside hiring, an added benefit for Parke-Davis.

Rezulin proved highly successful as well, though controversial because of deaths from liver toxicity. In 1998 worldwide sales were \$748 million, but dropped 10 percent last year to \$625 million, under use restrictions from the FDA. Warner-Lambert took the drug off the market this March 21 under pressure from the FDA.

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This form of alliance is a frequent occurrence. In today's marketing climate, industry analysts say, launch of a major new drug requires a field force of at least 3,000 representatives — more than most companies can assign to one product. The goal is to achieve a higher level of revenue more quickly and maintain a peak level longer (see High Compression Marketing, *Medical Marketing & Media*, March 2000, p. 66). The field force needed is achieved through alliances.

There are many recent examples of strategic alliances. In March, Bristol-Myers Squibb announced that it would co-promote its new antibiotic, Tequin, with Schering-Plough for respiratory infections. Schering-Plough has experience in the respiratory, allergy, and immunology markets. Bristol will focus on primary care. Knoll Pharmaceutical announced a co-promotion

agreement with Abbott Laboratories for its opioid and ibuprofen combination pain product Vicoprofen. "The goal is to leverage our respective organizational strengths," according to Knoll. Under the agreement, Abbott will promote the analgesic to markets in which it is strong — hospital-based physicians, emergency rooms, and surgical centers. Knoll will handle the office-based practitioners. These are just two examples, there are many others.

Joint ventures

This type of alliance requires formation of a stand-alone operating company with an explicit business strategy and organization. In the opinion of Pricewaterhouse partner Rule, it helps partners focus on the goals of the company. It can be set up to provide the liability benefits of a corporation and the tax benefits of a partnership.

Astra-Merck is a prime example of this type of alliance. A 50-50 joint venture of the two companies, it had exclusive rights to develop and market most Astra compounds. It was most impressive in successfully marketing its first product Prilosec, moving it from a so-so launch by Merck to the world's largest selling prescription drug. The company has undergone a number of changes in corporate identity and is now AstraZeneca. No reflection on its previous marketing skills.

Minority equity alliances

Usually, a major pharmaceutical company takes a minority equity position in a biotechnology firm to share technology and joint development of products. The alliance is a source of capital for a biotechnology company, particularly one without marketed products, as venture investors moved to Internet stocks in the past two years. It is a source of pharmaceuticals or technology platforms that speed screening and discovery for the drug firm.

A typical example is the relationship between Schering AG and Ribozyme

Pharmaceuticals, as explained by Eric Rule. The five-year collaboration will seek to develop ribozyme use to validate therapeutic targets and ribozyme-based therapeutics to treat a variety of diseases.

Schering invested \$5 million in Ribozyme Pharmaceuticals over the first year and will provide loans of \$2 million annually during the collaboration. Ribozyme also receives \$10 million in research funding and fees, up to \$35 million in earned milestone payments, and royalties on all products arising from the alliance.

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Ribozyme also has established partnerships in target validation with Chiron, Warner-Lambert, Pharmacia Biotech, and ALZA.

Research outreach programs

Sidney Taurel, president and COO, Eli Lilly has used what he called the emerging culture of alliances to reinvent R&D from deal making to partnership implementation. The re-engineering of research and development through partnerships has reduced the time in half from drug development to world marketing, from 4,800 days to 2,400 days.

Taurel was a keynote speaker at the Pharmaceutical Strategy Alliance Conference two years ago in New York, sponsored primarily by Windhover Information and Communitech Market Intelligence. Calling the new approach "research without walls," Taurel said "at Lilly we are blind to sources in filling research and development needs." At the time Lilly had alliances with ten companies developing technologies for screening, genomics, proteins, and delivery systems. It partnered with six companies in seeking productive targets and useful molecules involving neuroscience, three in endocrine diseases, and other companies in other therapeutic areas. The number of alliances has grown since.

Taurel was looking for higher probabilities of success, getting to market faster, lowering development costs, longer drug life cycles, and fewer competitors. As an example of the alliance strategy, Zyprexa got to market 18 months earlier than planned with a resulting increase in ROI.

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This past March, Regeneron Pharmaceuticals entered into collaboration with

Medarex to discover, develop, and commercialize human antibodies as therapeutics. Regeneron will contribute its expertise in discovering and characterizing proteins as drug targets, and Medarex will contribute its technology to create fully human antibody products for those targets.

Consortiums

This organizational structure involves participation of several companies, usually to form a development group. A clearly defined set of objectives and operating plan are needed for success. The ownership is spread among the participating parties and the cost is well defined and comparatively low.

An example: Ten of the world's top 20 pharmaceutical companies formed a consortium last year to support the major initiative of mapping the human genome. Each company contributed \$3 million, and the Wellcome Trust provided a grant of \$14 million, for a total of \$44 million to cover a two-year period. The consortium is working in conjunction with the U.S. government's Human Genome Project and, unlike most industry endeavors, the research results will be made public (see "How Competing Drug Companies are Cooperating to Develop New Gene Therapies," *Medical Marketing & Media*, August 1999, p. 68).

Many alliances underperform

The majority of alliances meet or exceed expectations. But 25 to 35 percent were described by company executives questioned as "underperformers." It is the human element rather than technical abilities responsible for less-than-satisfactory results, according to Pricewaterhouse. It surveyed 111 executives, vice presidents and above, mostly from pharmaceutical and biotech companies.

Differences in partner cultures was the top reason for alliance failures. Other factors were incompatible objectives of part-

ners, and poor alliance leadership or integration. Trustworthiness, fairness, and follow-through on deal commitments were considered to be the most important traits by survey respondents in considering potential alliance partners.

Innovative alliances

Partnerships for development of new drugs generally follow a familiar scenario. Usually a smaller, high-tech company discovers new technology. It is too risky for the small development company to go it alone. The financial risk involves the need

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for money for launch, infrastructure, etc. There is a lack of in-house expertise. Ramp-up requires high fixed costs that lead to limited or no profitability during early years of sales.

The commercialization alternatives are relationships with large pharmaceutical companies, out-licensing the new technology for a royalty or co-promotion for a profit share. "If a bio company gets to keep 50 percent of the profits in a pharmaceutical company co-promotion arrangement, even after taking all the R&D risk, that's about as good as it gets," said Louis G. Lange, M.D., Ph.D., chairman and CEO of CV Therapeutics (CVT), an internationally recognized expert in the molecular mechanisms of cardiovascular disease. The result is limited value creation in the biotech company for research or development programs.

Lange took a different approach. He made an alliance with Quintiles, the largest clinical research organization in the world, and its Innovex division, a sales and marketing organization. According to Lange, Quintiles completed more clinical trials, NDA filings, and product launches in 1998 than any other company. It had revenues of \$1.2 billion.

Innovex currently has 2,700 sales people, the sixth largest U.S. field force as of last year. It has experience selling seven cardiovascular products, which is what CVT is developing.

The product is ranolazine, an organic nitrate for preventing and treating angina pectoris, which works differently from other drugs in the category. It improves metabolism rather than dilating vessels. The present nitrate products include Imdur from Key Pharmaceutical and Isordil from Wyeth-Ayerst.

Imdur was used as benchmark for developing ranolazine marketing. It is for angina only, used alone or in combination. Imdur is the number-one selling, long-acting nitrate, with a 40 percent market share. Annual sales in the U.S. total \$250 million and fewer than 100 field representatives sell the product.

Ranolazine marketing will focus on 8,000 cardiologists and related physicians,

ALLIANCE BOOM SPAWNS NEWSLETTER

The significant increase in the number of alliances in the pharmaceutical industry has spurred publication of a monthly newsletter, *Pharma Agreement News*. Each issue reviews an average of 140 agreements signed or updated the previous month.

The newsletter is a spin-off of *International Pharmaceutical Agreements*, a searchable database on a CD-ROM with monthly updates giving full details of mergers and alliances. It details over 4,500 company deals since January 1997.

Both are published by Espicom Limited, West Sussex, UK.

requiring approximately 75-100 sales reps. Remaining prescribers will be targeted and reached with medical education materials, advertising, and direct mail.

The terms of CVT's "solution" are favorable. Quintiles/Innovex will provide and manage a dedicated sales force and fund other sales and marketing expenses. The value is more than \$110 million, subject to certain milestones. The sales force can be retained by CVT at the end of the term.

Innovex will receive up to one-third of U.S. revenues for five years, and a royalty for two more years. Since industry "best of class" costs for sales and marketing is 20-25 percent of revenues, the additional 10 percent payment of revenue to Innovex still leaves CVT with 90 percent of its profit on a 50/50 split, regardless of sales. CVT also receives from Quintiles an up-front equity, loan at NDA filing, and milestone at approval.

Ranolazine is now in Phase III trials, having completed one trial with 175 patients. It is now enrolling patients in a second one. An NDA is expected to be filed next year.

The arrangement is for U.S. only so that CVT can license ranolazine in Europe. The innovative relationship with a CRO/CSO

gives CVT substantial financing worth more than \$125 million, validation by a world leader, and acquisition of a dedicated sales force. The company will have no fixed sales or marketing expenses, significantly reducing commercialization risk. The ranolazine profit margin is 50 percent.

When push comes to performance

"New alliances are being forged with increasing speed to leverage clinical resources and market reach," in the words of an Executive Briefing from Anderson Consulting. "Historically, the top 15 pharmaceutical companies have delivered one NCE to market a year. ... Fewer than 25 percent of new products exceed \$500 million in peak sales, a common target for an acceptable return on R&D investments." Under present day economic circumstances, that business model is unacceptable.

A speed-up in average time to market is one expectation of large pharmaceutical companies, according to the Anderson

lessen the early clinical cycle time in Phases I and IIa by one-third, from 35 months in 1998 to 24 months in 2003. A faster full clinical development and regulatory cycle is expected to reduce the 44 months time span in 1998 to 37 months in 2003. One result would be an improved makeup of the industry's composite portfolio in future years.

The projected scenario increases average revenue per NCE from \$600 to \$640 million. Significant improvement in Phase I results in the overall clinical success rate, from a historic 10 to 1.1 up to 10 to 2.1. Companies expect to increase the number of NCEs brought to market from one to three this year and to four annually by 2008.

Given this new development and marketing model, alliances promise to be needed and fruitful. "The new model will require ... a variety of partnerships where collaboration and specialization add unique value," the Anderson report states.

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Improved screening of drug candidates and earlier elimination of doubtful compounds should bring a major reduction in the discovery/preclinical period, from code assignment to first dose in humans, from 28 months in 1998 to 16 months in 2003. Executives questioned say they seek to

advantage of web-based vertical alliances. ... Business development will play an increasingly important role in in-licensing development compounds. ... Science-based collaborative partnerships will develop and validate innovative methods which enable earlier, improved selection of compounds. And outsourcing service providers will significantly increase the efficiency by which clinical trial data are collected and managed." That covers all the bases. □

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