BY DENISE MYSHKO

IS BIGGER BETTER?

IT'S THE QUESTION THAT JUST DOESN'T GO AWAY.

A larger organization may be in a better position to survive attrition for a longer period, but in an industry where innovation is expected to be the driver of success for the long term,

BIGGER MAY NOT ALWAYS BE THE WAY TO GO.

Increased competition, more blockbuster products coming off patent, and a decrease in the number of new drug applications mean difficult times are ahead for the pharmaceutical industry. Are mergers the answer to support languishing pipelines? Industry experts say not always, as creativity and productivity from the R&D engine can get lost during the merger. And many say the expected synergies, especially in development, don't materialize in larger mergers; people and communication issues often can get in the way of achieving savings.

"Except for rare examples, as companies get larger, it's hard for them to be creative," says Carol Cherkis, Ph.D., life-sciences consultant, NewCap Partners Inc. "In a small environment where there is less bureaucracy and fewer rules, companies tend to have more creativity. From the standpoint of getting projects through the pipeline, bigger is not usually better."

During the BIO Investors Conference in February, Sean P. Lance, president and CEO of Chiron Corp., was quoted as saying: "Big mergers will not make the industry more creative. The mergers that we've seen haven't created the synergies that were first envisioned. Synergies in development have not been found because the projects already have been funded. And there are implications for harnessing innovation and creativity. First, the focus on innovation gets diverted over the merger period, for at least a year. Then companies are focused on filling the gaps, so R&D is further diverted. Then it is hard to make the move back toward innovation because the teams become unwieldy."

Mergers often create gaps that are hard to fill, says Lee Babiss, Ph.D., VP of preclinical research and development at Roche.

"In the end, when companies merge, two cultures that are very different are forced to become one," he says. "And in the process, the combined entity loses an enormous amount of productivity, from one to three years, as a consequence of bringing two very large diverse cultures together. This is largely driven from organizational confusion as it takes time to develop a single strategy to develop roles and responsibilities. And within a merged company, often there is duplication of roles and there is a need to remove that duplication."

An analysis by Bain & Company suggests that the companies that focused on and built strong positions through M&A in a few therapeutic franchises outperformed companies that followed a more broad-based approach.

From the standpoint of getting **projects through the pip eline**, bigger is not necessarily better.

DR. CAROL CHERKIS

Other industry leaders agree. "Stratospheric valuations on late-stage deals, combined with launch, promotion, and post-launch development costs that render uncertain the licensor's ROI — even from almost-certain billion-dollar products — have prompted the realization that sustainable franchises, not single blockbusters, will be the key to success in the future, and that no single blockbuster — no matter how large — constitutes a franchise," says Ed Saltzman, president of Defined Health.

Mr. Saltzman says companies will have to concentrate their commercialization efforts on multiple products within disease areas as a way to maintain a competitive advantage.

"We will no doubt see more deals that seal a company's future in a particular therapeutic franchise area for the next 15 years or 20 years, or at least increase its chances to be a strong player," he says. "All these aspects are now shifting the focus to early-stage in-licensing and M&A."

According to a white paper from GartnerG2, a research service of Gartner, mergers and acquisitions are no longer the growth weapon they once were. Gartner researchers say mergers and acquisitions aren't obsolete, but they no longer are the only option for growth and may, in fact, introduce inefficiencies that slow growth.

According to Gartner's analysts, a few dominant companies will continue to pursue a "bigger is better" strategy to take advantage of the economies of scale. The rest, however, will compete on "economies of scope" — delivering value through alliances, licensing deals, and targeted acquisitions as a way to acquire pipeline assets and build stronger positions in certain therapeutic areas.

Mr. Saltzman says the benefits of size are increasingly being questioned.

"In a business that is characterized by attrition, being bigger is one clear advantage," he says. "But if being bigger decreases a company's ability to discover new drugs because its size makes it too bureaucratic and it can't attract creative people, then being bigger becomes almost silly."

"Companies have to keep the investors happy and meet investor demand for double-digit earnings growth," says Theresa O'Connell, an industry analyst with Frost & Sullivan. "That is one of the drivers for the industry consolidation that we've seen in the past 10 years. Mergers and acquisitions are one way to prop up the pipelines so that they appear to look a little more promising."

Investors, Mr. Saltzman says, have determined that the pharma industry should be valued as a growth industry and should perform to expectations.

The Top 10 Deals in 2002*

1. $59,515 **Pharmacia** acquired by **Pfizer**
2. $1,126 **Nycomed Pharma (CSFB, Blackstone NIB)** acquired by **Investor Group**
3. $851 **Lek (99.1%)** acquired by **Novartis**
4. $467 **Triangle Pharmaceuticals** acquired by **Gilead Sciences**
5. $380 **Immunex, Leukine business** acquired by **Schering**
6. $360 **Elan-Abelcet rights in U.S., Canada,and Japan** acquired by **Enzon**
7. $345 **Viatris** acquired by **Advent International**
8. $320 **Tibotec-Virco** acquired by **Johnson & Johnson**
9. $305 **Wyeth-ESI Lederle Assets** acquired by **Baxter Healthcare**
10. $295 **Eli Lilly-SeraFem Rights in U.S.** acquired by **Galen**

* Includes mergers, product acquisitions, and private equity
Note: Dollars are in millions.
Source: PricewaterhouseCoopers, New York, February 2003.
For more information, visit pwcglobal.com.

"Pharma CEOs are captivated by that," Mr. Saltzman says. "The bottom line — and the reason why I don't think we'll see many more mergers — is it's just not possible to pop out enough blockbuster drugs to grow at the level that investors expect — a minimum of 10%."

Following the trend toward building expertise in therapeutic categories is the example of the Pfizer/Pharmacia merger, Mr. Saltzman says. "Pfizer is acquiring a presence in a new area — oncology," he says. "Once this merger closes, Pfizer will have Pharmacia's more than respectable oncology business, which will give Pfizer an entry into that very complex category. It also will give Pfizer a brand franchise in ophthalmology, one that very few pharma companies enjoy. Mergers can be used as a way for companies that have too few therapeutic franchise areas to acquire new ones."

The franchise strategy is exactly what managers at companies such as Solvay Pharmaceuticals Inc. are employing. Solvay Pharmaceuticals looks at mergers and acquisitions strategically, says Joseph Feldhouse, VP of business development at Solvay Pharmaceuticals.

"We are looking to acquire marketed products, pipeline products, and/or companies that fit with our focus," he says. "We are also doing targeted discovery alliances."

Solvay specializes in four therapeutic areas: psychiatry, gastroenterology, hormone replacement therapy, and cardiology. In each of these therapeutic fields, R&D activities focus on carefully selected clinical targets.

To this end, Solvay Pharmaceuticals recently acquired worldwide rights, excluding Japan, to cetrorelix for the treatment of endometriosis and uterine fibroids in women and benign prostatic hypertrophy in men. Cetrorelix is a gonadotrophin releasing hormone antagonist (GnRH antagonist). Its effect is to inhibit the release of sex hormones, and this reduction in sex hormone levels may be beneficial in the indications under study. Phase II clinical programs in the three indications are ongoing at Zentaris, a German biopharma company.

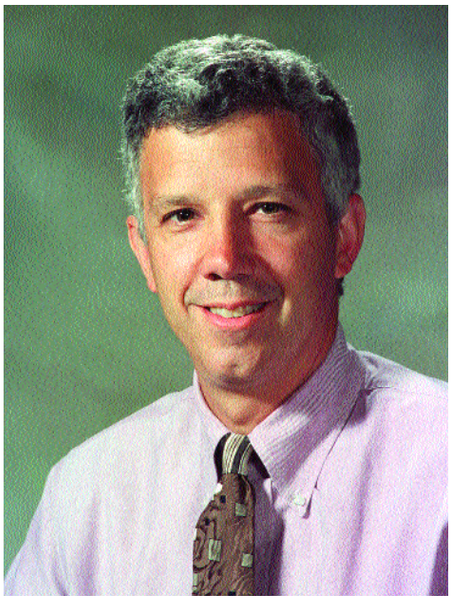
"We will always search for products that help more patients rather than garnish the most dollars," Mr. Feldhouse says. "I don't want to sound altruistic, but our focus is on patient and physician audiences rather than size. We've had incredible growth by maintaining this strategy. For us, a blockbuster drug may generate a few hundred million dollars, although many companies could argue that this wouldn't be considered a blockbuster in today's world. For us, a blockbuster drug is one that makes an absolute difference in how physicians treat disease."

Furthermore, according to analysts, because traditional drug-discovery technologies are not yielding as many drugs as they used to, companies are being forced to look beyond blockbuster categories.

"All the obvious diseases are well-understood, and they are relatively effectively treated today," Ms. O'Connell says. "It's becoming more and more difficult for companies to develop a drug that is differentiated from the gold standards already on the market."

She says this forces companies to look at some of the other less-understood diseases that they might not have spent time on in the past.

"Companies need to do smart and innovative R&D to be able to address unmet medical needs," Ms. O'Connell says. "This requires enormous R&D budgets. To remain in the game, the number that we've been hearing from pharmaceutical companies is an R&D budget of at least $1 billion. This has been one of the reasons for mergers and acquisitions."



Mergers often create **gaps** that are hard to fill.

DR. LEE BABISS

Equity Investments: An Alternative to M&A

WHAT IF A COMPANY COULD GET SOME OF THE SAME BENEFITS OF AN ACQUISITION — ACCESS TO NEW TECHNOLOGY, PIPELINE ASSETS, AND POSSIBILE ADDITIONAL REVENUE FROM PRODUCT CANDIDATES — WITHOUT ACTUALLY BUYING A COMPANY?

A big part of Roche's strategy for its research and development includes making equity investments in promising companies, as well as pursuing individual collaborations and alliances and acquisition candidates.

"The beauty of an equity investment is that the company being invested in still is able to retain its culture," says Lee Babiss, Ph.D., VP of preclinical research and development at Roche. "Essentially, the investor company is betting on that culture, on the management team that's in place, and on the business model to drive future productivity."

This, he says, creates a hub-and-spoke organization for Roche, with its own pharmaceutical and diagnostics divisions as the hub, and in companies such as Genentech, Chugai, Basilca Pharmaceuticals, and Antisoma as the spokes.

"Roche's investment is realized in two ways," Dr. Babiss says. "Our company realizes growth from the actual equity, as well as from the licensed products that our company sells in various markets. For example, Genentech markets its products in the United States; Roche has rights to these everywhere outside the United States. Through this arrangement, we get two returns on that investment. We get the revenue that is generated from the products — Herceptin as an example — everywhere outside the United States, and because of our equity investment, we get a percentage of the return on investment from the U.S. market."

Dr. Babiss says this model may not appeal to all companies, however.

"It's appealing to be in control," he says. "One of the aspects a company gives up with an equity investment is that it doesn't have ultimate control of the decisions being made and the direction of that given company. The investing company can exert some influence, but it doesn't have total control. But, by being thoughtful and strategic in the equity investment, control really isn't an issue. It's the output and productivity that we're interested in."

According to Frost & Sullivan, R&D spending by pharma companies has increased by more than 200% in the last decade, and since only one in three drugs recuperates its development costs, keeping up this level of investment is becoming more challenging.

In 2001, PhRMA member companies invested an estimated $30.3 billion in R&D. This represents a 16.6% increase over expenditures in 2000. PhRMA member companies spent an estimated 17.7% of sales on R&D.

But this increased spending hasn't resulted in enough new products to offset the loss of revenue from products losing patent protection.

Pharma industry pipelines, and especially big pharma pipelines, are weak, says Elgar Peerschke, VP and head of the North American Healthcare Practice at Bain & Company.

"By going through the top 20 pharmaceutical companies, we'd have a hard time saying this is one of the richest pipelines in the history of the industry by any stretch," he says.

To come to this conclusion, Mr. Peerschke evaluated two areas: whether the product meets unmet needs and whether it has blockbuster potential.

"That said, I don't think it's the end of big pharma or value creation in pharma," Mr. Peerschke says. "There is a great deal of good innovation going on inside big pharma, arguably not enough. But there also is innovation outside big pharma — in academic centers, in biotech, etc. The good news for pharma companies is, if nothing else, they have a clinical and commercialization engine that these other entities need to leverage."

Mergers can be used as a way for companies that have too few therapeutic franchise areas to **acquire new ones**.

ED SALTZMAN

The M&A Scene

Globally, there were 374 merger and acquisition deals announced in the pharmaceutical sector in 2002, which was a 12% increase from the number of deals announced in the previous year.

PricewaterhouseCoopers' latest analysis of deal activity in the pharma sector shows that the average value of deals in 2002 was substantially lower than in 2001. Excluding Pfizer's proposed $60 billion combination with Pharmacia, the total deal value was $11 billion, compared with $61 billion in the previous year.

Among the top 10 deals in 2002, two trends are evident, say PricewaterhouseCoopers' analysts: the dominance of product-based deals and the incidence of private equity-backed acquisitions.

"Product acquisitions are a back-to-basics approach to fill the pipeline," says Curt Cornwell, partner at PricewaterhouseCoopers. "This trend will continue and probably increase. The pharmaceutical industry is renowned for alliances and a variety of licensing agreements and to some extent joint ventures, which are ways to enhance pipelines."

PricewaterhouseCoopers researchers say the key drivers behind M&A in the pharmaceutical sector in 2002 were: big pharma companies needed to fill their R&D pipelines and replace drugs coming off-patent, and biotech companies needed access to cash to develop their products and bring them to market.

"In that realm, there may be more pharma/biotech mergers, such as Johnson & Johnson's acquisition of Scios," Mr. Saltzman says.

J&J agreed to acquire Scios for $2.4 billion. Scios is a biopharmaceutical company that develops novel treatments for cardiovascular and inflammatory disease. Through the acquisition, J&J gains access to Scios' product Natrecor, the first novel agent approved for congestive heart failure (CHF) in more than a decade. Natrecor is a recombinant form of a naturally occurring protein secreted by the heart as part of the body's response to CHF.

In addition, according to research by Cutting Edge Information, the industry is expected to enter into more partnerships with biotechnology firms, such as the recent $32 million OSI Pharmaceuticals deal with Cell Pathways.

The largest pharma-biotech deals have steadily increased in value in recent years — from SmithKline Beecham's $125 million deal with Human Genome Sciences in 1993 to the $500 million Bayer-Millennium Pharmaceuticals alliance in 1998 to the $1.3 billion alliance between Bayer and CuraGen in 2001.

Patent Challenges

Offsetting lost revenue from pending expirations of blockbuster products, according to some analysts, has been a significant driver of M&A activity. Blockbuster products with collective U.S. sales of more than $36 billion will lose market exclusivity in the next four years, according to analysts with Frost & Sullivan. Lovenox, Prevacid, Pravachol, Zocor, and Zoloft are few of the major blockbusters that are expected to lose their market exclusivity within the next three years.

According to industry stats, the average time of patent protection is about 12 years.

"This is expected to drop to about 10 years within the next decade," says Ajit Baid, pharmaceuticals industry manager at Frost & Sullivan. "The life span of drugs is becoming shorter and shorter, and companies have to contend with much more competition in all therapeutic areas than in the past. For example, one of the biggest drugs of the last three decades is Wyeth's beta blocker, Inderal. Inderal had 13 years of market exclusivity before the first me-too drug came on the market. A drug such as Celebrex on the other hand, the first of the COX-2 inhibitors, was only on the market a few months before a similar drug entered the market."

"Shrinking market exclusivity is squeezing company profits," Ms. O'Connell says. "When a new class of drug was brought to the market in the past, it might have been the only one of its type for years. Today, drugs such as Celebrex, which was revolutionary when it entered the market, faced competition two months later when Vioxx came to the market. Companies don't have years to recoup their development costs. Almost right from the start they are facing competition."

Part of the problem is the longer development time of new drugs, Mr. Baid says.

"In the 1960s, the average drug development time was eight years, which has increased to approximately 14 years today," he says. "The increase in the drug development time is due to the higher standards set by the FDA for

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JOSEPH FELDHOUSE

drug approval, plus the fact that there are fewer opportunities in diseases that are well-understood and effectively treated. Therefore, scientists have to work hard to develop drugs that are sufficiently differentiated from products that already exist in the market. Or scientists have to tackle complex diseases that are not well-understood; this may require complex and innovative research and development."

Despite R&D spending increases, analysts have not observed a substantial increase in new product flow.

"As a general rule the industry does not have the pipeline power to replace the huge drugs that are going to go off patent in the short term, which is all anyone really knows about," Mr. Saltzman says. "There is a great deal of promise in the early-stage development. The problem is that the pharmaceutical industry is a business of attrition and all things look promising at an early stage. Are there going to be huge fruits that come from innovations in our understanding of the genome and proteomics? You would have to be a real committed pessimist to say wonderful things won't come from those efforts. The big question is when."

The slowdown in R&D proficiency is readily visible, according to industry analysts. In 2002, the Food and Drug Administration received 23 NDAs for innovative drugs in 2002, down from 30 in 2001. In 2002, the FDA approved 17 new molecular entities (NMEs). This was down from 24 NMEs in 2001.

"Companies are being very creative about product life-cycle management," Ms. O'Connell says. "For instance, companies are developing extended-release versions of a product, or drugs that have received approval for a pediatric indication. This is not really innovation, companies keep milking the old cash cows until new generation drugs make it to the market."

Life-cycle management is a tried-and-true method to protect a blockbuster product from generic competition for as long as possible.

All of this has implications for pharma. Patents are important to firms' R&D efforts. Absent patent protection, or some equivalent barrier, imitators could free ride on an innovator's FDA approval and duplicate a compound for a fraction of the originator's costs. ✦

PharmaVoice welcomes comments about this article. E-mail us at feedback@pharmavoice.com.

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