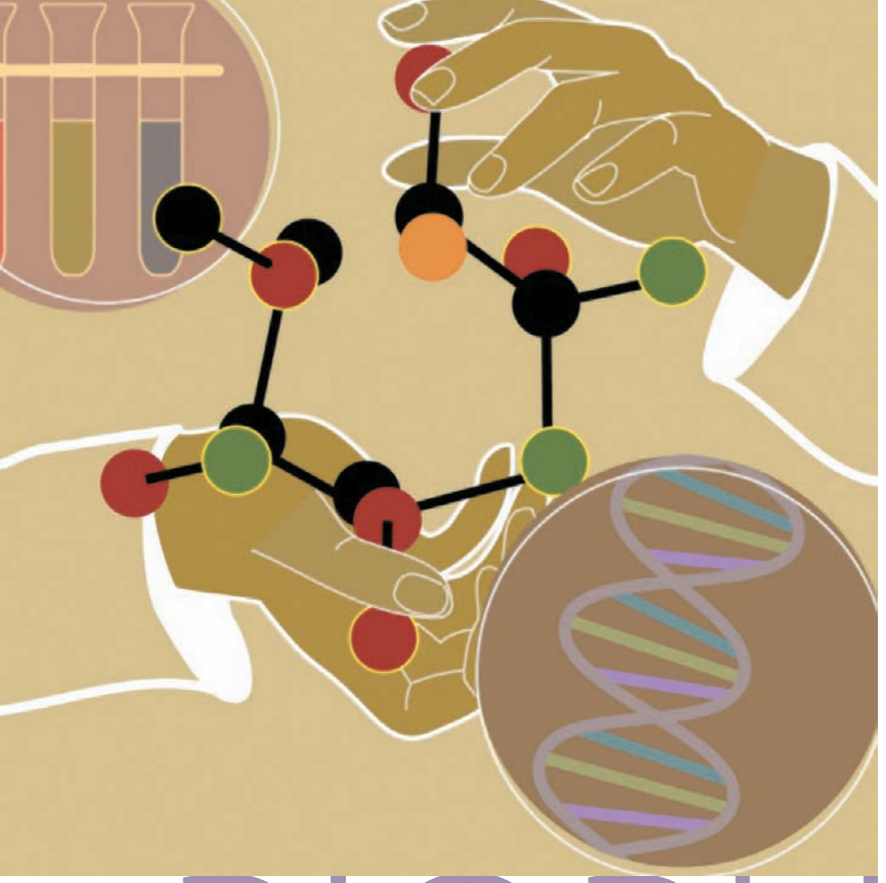


BY DENISE MYSHKO

BIO Meets PHARMA to Form the New Age of BIOPHARMA

THE DISTINCTION BETWEEN BIOTECH AND PHARMA IS BLURRING.

The result: broad-based companies use their expertise in a disease and the underlying science to choose the most appropriate approach, whether small molecule or biologic, to create new therapeutic interventions.

The pharmaceutical and biotech industries are gradually integrating into one biopharmaceutical industry. In a white paper released in May 2005 by the Life Sciences and Health Care practices of Deloitte, it was surmised that the distinction between biotechnology and pharmaceutical firms will erode over the next decade

Strictly speaking, the term "pharmaceutical" refers to medicines composed of small, synthetically produced molecules. "Biotechnology" products are typically large molecules developed through cellular and biomolecular technologies that capitalize on the attributes of cells, DNA, and proteins. Some say the pharmaceutical industry's pipeline hinges on the R&D efforts of biotech companies. Large pharma companies are seeking more alliances with biotech through acquisition or licensing agreements, with such alliances rising to 502 in 2004 from 69 in 1993, according to a Deloitte Consulting study, Critical Factors for Alliance Formation.

In fact, half of the therapeutic biologics registered with the Center for Biologics Evaluation and Regulation of the FDA now belong to pharmaceutical companies.

This trend is further backed by researchers at Ernst & Young, who say 2005 was a notable year for mergers and acquisitions with a marked increase in pharma-biotech deals. The increase in accords is being driven, they say, by pharma's need to strengthen its pipeline in the face of patent expirations, pricing pressures, and competition from specialty pharma.

CHANGE IN THE AIR

Certainly, some pharma companies have had their hands in biologics for some time, but now experts say companies are beginning to make drastic changes in their business strategies and how their companies are structured to pursue the promise of biopharmaceuticals and as a way to leverage expertise in a therapeutic disease area.

DR. BOB STEIN ROCHE

○ If companies have expertise in a disease and the underlying science, THEY CAN PICK THE BEST INTERVENTION AND USE THE BEST APPROACH TO CREATE A NEW MEDICINE THAT HAS THE BEST CHANCE OF SUCCESS.

The convergence has started to gain momentum based on two factors: the complementary therapeutic platforms that are being used by pharma and biotechnology companies and the therapeutic areas being pursued.

"Historically, the innovative and more risky science had been the paradigm of the biotech industry," says Louise Makin, CEO of BTG Plc. "Now big pharma companies, whose primary domain was marketing, are working in some more cutting-edge areas of research. The overall science is getting tougher and tougher, and it's harder to bring a new drug to market."

At the same time, biotech companies are adopting small-molecule approaches, typically the bread-and-butter of pharmaceutical research, to move into selected therapeutic areas. For example, industry leaders say Genentech, which traditionally has been in the protein therapeutics space, is now entering the small-molecule space.

"Most of the big pharmaceutical companies have realized it's important to have large-molecule products in their pipelines," says Ben Bonifant, leader of the business development practice at Campbell Alliance. "Interestingly, some of the traditional biotech companies are moving in the other direction toward small-molecule development.

"The definition of biotech may change, and big pharma will start to internalize some of the research activities that biotech companies have been doing on the more proven technologies," he says. "But there will still be interesting science, often coming out of an academic setting, being fed by private equity and venture capital until it reaches the point of interest by a company that can, and wants, to commercialize the application."

This blurring of the lines between pharma and biotech, he says, is about applying capabilities and adjusting the business model to capitalize on different pieces of the market.

"This not a full-scale change or transition of the business model, but more of a migration," Mr. Bonifant says.

Deloitte researchers say widespread pressure to lower prices, along with increased competition, will speed up consolidation and convergence between the two sectors. Companies need to form a new ecosystem based on acquisitions, mergers, alliances, and exploratory relationships in emerging markets.

"Big pharmaceutical companies are not only looking to beef up their pipelines but also to diversify into other technology platforms as a way to improve their market opportunities," says Glenn Snyder, principal with the life sciences and healthcare practice at Deloitte Consulting.

According to Deloitte, companies that are able to harness both the innovative culture typical of biotech companies and the operating capabilities and management processes more characteristic of pharmaceutical firms will be positioned to sustain strong revenue growth and exceed shareholder expectations in the coming years.

Deloitte researchers say successful companies will be differentiated by their ability to target new opportunities through innovation based on unique sets of intellectual property and their ability to extend core capabilities.

Bob Stein, M.D., Ph.D., president of Roche Palo Alto LLC, says convergence requires careful consideration of several factors.

"There has to be a true unmet medical need, the right target needs to be chosen, the right clinical studies need to be done to show the potential benefit, the safety issues have to be considered in perspective, and the project has to be strategically important to the company," Dr. Stein says.

Roche has invested heavily in biologics over the past 15 years or so, first acquiring a majority interest of Genentech Inc. in 1990, acquiring PCR technology from Cetus Corp. in 1991, and then buying Boehringer Mannheim in 1998 for its diagnostic capabilities.

In the future, the prediction is that companies will be able to provide integrated healthcare solutions built on a platform of intellectual property instead of on therapeutic drugs alone. New insights into specific diseases and new diagnostic/prognostic technologies will

INDUSTRY TRENDS

○ **Growing business pressure will speed up consolidation and pharma-biotech convergence.**

Pressure from consumers and governments to slow the increase of healthcare costs, along with new competitors, will drive structural changes in the industry. Established firms will face strong competition from emerging markets, as companies in these markets evolve from outsourcers and generic drug producers to become formidable competitors.

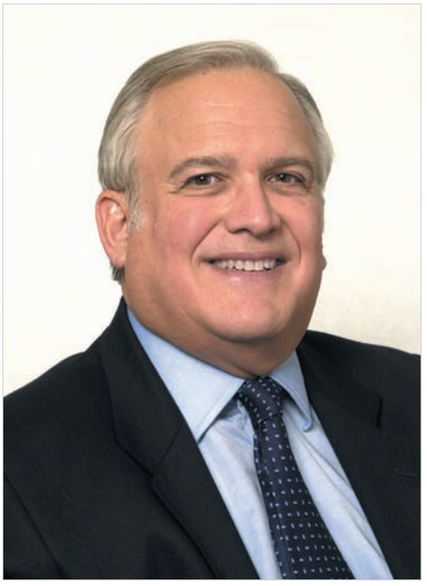
○ **Asian life-sciences markets will expand faster than American and European markets.**

China and India will exceed 15% revenue growth annually over the next decade, outpacing growth rates in the United States, Japan, and Western Europe, which are projected to increase at 10% or less annually.

○ **The recent decline in the industries' reputations is a matter of great concern.**

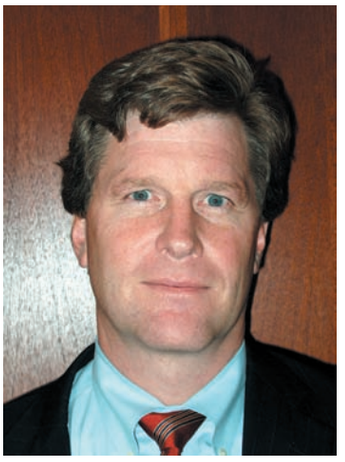
There is a belief that the erosion of corporate reputation will affect long-term revenue growth. Some industry leaders are worried this problem will result in more government regulation, but they are hopeful that since the damage was self-inflicted, it can be remedied.

Source: Deloitte, New York. For more information, visit deloitte.com.



BILL KRIDEL FERGHANA PARTNERS

○ Acquisitions are about acquiring skills and new ways of addressing the same disease WITH NEW AND BETTER TOOLS.



BEN BONIFANT CAMPBELL ALLIANCE

○ ONE CHALLENGE WITH MERGERS IS MELDING THE DIFFERENT CULTURES OF THE COMPANIES. Even the big biotech companies have a different culture from traditional pharma companies.

redefine a drug's value by better aligning the right regimen to the right patient group.

There has already been some move in that direction. Roche's experience in biotech development includes its product Pegasys and its companion hepatitis virus detection system, which have been cited as examples of integrated prognosis and therapeutic solutions.

Pegasys, a pegylated alpha interferon, was approved by the FDA in 2002 for use in combination for the treatment of adults with chronic hepatitis C who have compensated liver disease and have not previously been treated with interferon alpha.

Since launching its first hepatitis C test in 1993, Roche commercialized several tests for hepatitis C detection and viral load monitoring in the ex-U.S. market. In July 2001, two of these tests — Amplicor HCV Test v2.0 and Cobas Amplicor HCV — received FDA approval. Both detect the presence of hepatitis C RNA (ribonucleic acid) in human serum and plasma, which indicates active HCV infection.

Another often-cited example is Genentech's Herceptin/HER2 test, which was approved in September 1998, for the diagnosis and treatment of HER2-positive metastatic breast cancer. Herceptin is designed to target and block the function of HER2 protein overexpression.

Helene Ellison, president and CEO of HealthStar Public Relations, says the focus of pharma's attention on the biotech industry is shifting from pure science to commercial opportunities.

"A few years ago, technology platforms were of interest; now the focus is on pipeline opportunities," she says. "Companies with exciting pipelines are receiving the backing and attention from the financial community and from the pharma community."

THE STAGE IS SET

The protein therapeutics market has more than doubled in the last five years, jumping to $51 billion in 2005 from $25 billion in 2001, according to the latest market research from Kalorama Information.

The report, The Protein Therapeutics Market: The Science and Business of a Growing Sector, predicts that sales by 2010 should reach $87 billion, powered by heavy demand and rapid sales in the United States and Europe, which currently account for more than 80% of the market.

New product innovations, respectable margins, and relatively mild pricing pressures compared with the rest of the pharmaceutical market will continue to be strong market drivers.

An August 2006 report from the Pharmaceutical Research and Manufacturers of America (PhRMA) states that there are 418 medicines and vaccines developed through biotechnology now being tested to treat more than 100 diseases.

The biotechnology medicines include 210 medicines to treat cancer, 50 to treat infectious disease, 44 to treat autoimmune disorders, 22 to treat HIV infection and related-conditions, and 22 to treat cardiovascular diseases.

"There are certain diseases that are more amenable to biological therapeutics than small molecules," says Bill Kridel, founder and managing director of Ferghana Partners Group. "The world of proteins, peptides, and oligonucleotides will address different types of targets more readily than little while pills. There are potentially billions of dollars in sales from biologicals beyond those already on the market."

According to Mr. Stein, some targets are only approachable with small molecules. For instance, intracellular enzymes that are involved in signal transduction, such as kinases or nuclear hormone receptors, and some targets are only approachable by biologics at this point. Additionally, certain surface features of cells that participate in protein-protein interactions are too big to block the small molecules.

"Biological blocking agents (either antibodies or decoy receptors) are also applicable for neutralizing circulating agents such as an interleukin or a cytokine," he says.

Mr. Kridel says this means many biopharma companies will need two regulatory departments, not just one.

"At the very top of the industry, there will be a few people and companies who are familiar with both small-molecule and biologic clinical development and regulations," he says. "The same thing will be true with manufacturing. There will be a manufacturing plant that turns out pills and another one that turns out peptides."

As many pharmaceutical companies position themselves to take advantage of new therapeutic interventions and high-growth opportunities that large molecules afford, they will likely need to outsource some of their clinical development to companies that have experience with biologically based products.

John Watson, VP of corporate marketing and sales at Covance Inc., says, as such, there likely will be a higher demand for integration of CRO services through strategic partnering.

"Pharma companies that are filling their pipelines through mergers and acquisitions

now have a greater need to outsource to CROs as a way to reduce their internal R&D expenses, improve their quality, reduce their timelines, and meet regulatory submission objectives," he says.

RECENT MOVES

While Roche has been investing in biologics for some time, the company has recently made the decision to invest even more in its therapeutic protein initiative.

Roche has significant core expertise in the generation of antibody and other protein reagents and the preparatory preclinical work required to evaluate them for use. The company's core facility for this business unit is located in Penzburg, Germany. Researchers work in close collaboration with the disease-area experts at the various Roche research campuses worldwide.

"For example, our global inflammation, autoimmunity, transplant, virology, and neurosciences group is in Palo Alto," Dr. Stein says. "There's a lot interest in surface molecules that are involved in the control of white-cell functions and in small-protein messengers; these are used to talk to each other and influence body function. These are great targets for antibody interventions."

He says the biologic and small-molecule discovery programs are integrated within Roche Pharmaceuticals.

"The early-development portfolio and the late-development portfolio include a mix of small-molecule and protein therapeutics," Dr. Stein says. "These are looked at as part of our common portfolio, which allows us to diversify our risks and to have a more productive and balanced range of opportunities. This structure allows us to do what we're dedicated to do: find the best possible medicines for each medical need that we're trying to address."

Another company investing heavily in biologics is Wyeth Pharmaceuticals. The company has overhauled how it does business and is structured to pursue the promise of biopharmaceuticals. The company has emphasized a sustainable new paradigm, which combines the biotech culture with the resources and global reach of a large pharmaceutical company, a model company executives say is required for success in a challenging and changing industry.

In an interview at the recent DIA meeting, Cavan M. Redmond, executive VP and general manager of BioPharma at Wyeth Pharmaceuticals, told PharmaVOICE that biopharmaceuti-

GROWTH IN GLOBAL BIOTECHNOLOGY 2004-2005

	2005	2004	change%
Public companies			
Revenue	$63,156	$53,367	18%
R&D expense	$20,415	$19,542	4%
Net loss	$4,388	$6,270	30%
No. of companies			
Public companies	671	645	4%
Private companies	3,532	3,522 0	0.3%
Public and private	4,203	4,167	1%

Note: Dollars are in millions
Source: Ernst & Young, New York. For more information, visit ey.com.

HELENE ELLISON HEALTHSTAR PUBLIC RELATIONS

THIS IS AN INTERESTING TIME BECAUSE EVERYTHING IS ABOUT THE PIPELINES. IT'S ALL ABOUT THE PRODUCTS.

The promise for pharma companies lies in the pipelines they are acquiring from biotech.

cals will be a big portion of pharma's — and specifically Wyeth's — total business.

"To achieve this goal, companies will have to make drastic changes in the way they do business, since biotech products are an entirely new way of developing products," Mr. Redmond says.

Wyeth leaders expect that by 2012, biopharmaceuticals will make up 25% of the company's total business.

The centerpiece of Wyeth's investment in biotech processes is an integrated biotech production facility in South County Dublin, Ireland. The facility, which opened in September 2005, is a 1.2 million-square-foot campus, one of the largest integrated biotech manufacturing facilities in the world.

Wyeth invested almost $2 billion in the Grange Castle facility, which comprises three separate facilities: a drug development unit, a drug substance site, and a drug product facility. These facilities go into production on a phased basis in the next four years.

Among the biotech products that will be produced at Grange Castle is the anti-arthritic treatment Enbrel, for which Wyeth owns the rights outside the United States. Prevenar, a pneumococcal 7-valent conjugate vaccine, also is scheduled to be produced at Grange Castle, as is Tycagil, an intravenous (IV) antibiotic.

In May 2006, Merck & Co. acquired two companies to further enhance its capabilities in biologics research and development.

Merck acquired Abmaxis Inc., a privately held biopharmaceutical company dedicated to the discovery and optimization of monoclonal antibody (MAb) products for human therapeutics and diagnostics, for $80 million in cash. The deal makes Abmaxis a wholly owned subsidiary of Merck.

Under an agreement that Merck established with Abmaxis in late 2004, Abmaxis successfully re-engineered a Merck human monoclonal antibody and improved antibody affinity more than 70-fold while retaining its specificity. Merck executives say the success of that collaboration was a key factor in acquiring Abmaxis.

Merck also acquired GlycoFi Inc., a privately held biotechnology company in the field of yeast glycoengineering and optimization of biologic drug molecules, for about $400 million in cash.

Merck executives say GlycoFi's scientific expertise, patent estate, and robust technology platform are significant steps toward enabling Merck to discover, optimize, and develop novel biologic drugs.

This could be useful in discovering therapeutics for oncology, as well as novel vaccines for infectious diseases. Oncology and novel vaccines are two of nine priority disease areas of research for Merck.

Glycoengineering allows for the manufacture of proteins, such as monoclonal antibodies, with prespecified and defined human carbohydrate side chains. The ability to make such proteins in yeast has advantages of speed, cost, and quality over current methods of producing monoclonal antibodies and other protein therapeutic agents. ✦

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

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