BY DENISE MYSHKO

The Art of the Deal

The biotech industry is in a much stronger position now than it was in its early days, **AND TODAY BIOTECH COMPANIES ENJOY A PROMINENT SEAT AT THE NEGOTIATION TABLE.** Biotech companies, especially those with products, are asking for true collaboration instead of relying on licensing deals.

THE DAYS OF BIOTECH BEING THE POOR COUSIN OF THE LIFE-SCIENCES INDUSTRY ARE OVER. TODAY'S BIOTECHNOLOGY COMPANIES HAVE ACHIEVED A LEVEL OF DEAL-MAKING SOPHISTICATION IN KEEPING WITH THEIR GROWING INFLUENCE ON THE PHARMACEUTICAL INDUSTRY, ACCORDING TO A RECENT REPORT FROM IBM INSTITUTE.

What's more, competition for alliance deals has intensified. The more mature biotech companies are in a position to compete alongside longer-established pharma companies for a slice of the $6.5 billion per year biopartnering pie. According to the results of IBM's recent BioPartnering survey, more than half of the companies identified by biotechs as alliance partners were not from the top 10 pharma companies. In fact, the number of biotech-biotech deals signed between 1996 and 2003 has doubled.

"We've been conducting this survey for five years, and the number of deals is increasing, although slowly, for a couple of reasons," says James W. Cortada, Ph.D., a team leader at IBM Institute for Business Value, IBM Business Consulting Services. "One reason is that the pipelines of the large pharma companies are fairly empty so they are exploring the opportunities that biotech has to offer."

Another reason, he says, is that the industry is slowly beginning to shift away from the blockbuster model.

"As the number of nonblockbuster products — specialized products for niche areas — increases to fill the pipeline, so too will the number of pharmaceutical partnerships and transactions with biotech companies," Dr. Cortada says. "And of course, there is the issue of expanding the different relationships across the entire value chain, which is being driven by the large pharma companies as they evaluate ways to drive down operating costs across their entire enterprise."

One of main reasons pharma companies are driving down costs is because many of their main revenue generators have become open to generic competition.

"As everyone in the industry knows, most of the major pharma companies have large blockbuster drugs coming off patent over the next five years," says Tracy Lefteroff, global managing partner, life-sciences industry services, at PricewaterhouseCoopers. "This trend is changing the collaboration model. Pharmaceutical companies have begun to acquire biotech companies as opposed to just partnering with them for certain drugs. This trend will continue because biotech companies don't need a partner to take a drug to market."

Also contributing to biotech's more powerful position at the negotiating table is the relative financial strength of many of today's companies.

"Biotech companies are less desperate for cash today," Mr. Lefteroff says. "Biotech companies are finding that there is ample money available in public markets and through private venture capital. And because these companies are less anxious for cash, they're not forced to license away the crown jewels to pharmaceutical companies as they were 10 to 15 years ago."

Another major strength for biotech companies is the broadening technologies that they have developed for drug discovery, says Keith Redpath, Ph.D., head of the life-sciences research team at Wood Mackenzie.

"It would be impossible for pharma companies to establish these same technologies in-house," he says. "By participating in as many drug-discovery technology deals as possible, companies are essentially hedging their bets as to which one is going to deliver."

The biotech industry has matured, says Anna Protopapas, VP of corporate development at Millennium Pharmaceuticals Inc.

"The industry has generated a lot of products and continues to be a source of innovation," she says. "Big pharma is looking to biotech for new products and innovation. And that creates

THE PERCEPTION ABOUT THE POSITION OF STRENGTH OF BIOTECH relates to the needs of big pharma companies to acquire later-stage products to fill their pipelines. They are looking for Phase III primary-care products that could have peak sales in excess of $2 billion.

DR. FRANK ARMSTRONG

For the attractive late-stage products, there is heavy competition and the stakes go up. EARLIER-STAGE OPPORTUNITIES ARE USUALLY MORE AFFORDABLE.

DR. THOMAS HOFSTAETTER

fertile ground for new types of deals and new types of relationships."

This is certainly true in Millennium's case.

"In the last decade, what has changed is the type of deal that meets our strategic needs," Ms. Protopapas says. "When the company was young, we formed partnerships during the very early stages of research. We discovered genes and targets, and we licensed them to our partners to take forward into the clinic and on to the market. As Millennium has matured, our partnerships have matured. We now jointly discover, develop, and commercialize products with partners in the United States, and these partners commercialize the products outside the United States. More recently, we've negotiated two deals where we retain the U.S. market rights and our partner has commercialization rights outside the United States."

One of these recent deals is with Johnson & Johnson for Velcade, which received accelerated approval in May 2003 in the United States for the treatment of relapsed and refractory multiple myeloma. Velcade is being codeveloped by Mil-

THREE LINES OF ALLIANCE CHANGE

TODAY'S BIOTECH COMPANIES DISPLAY UNPRECEDENTED AGILITY IN MANAGING A RANGE OF OPPORTUNITIES, FROM SIMPLE ONE-OFF PROJECTS TO COMPLEX MULTISTAGE DEALS. AS A RESULT, THE DYNAMICS OF ALLIANCE-MAKING IN THE DRUG INDUSTRY ARE CHANGING ALONG THREE POTENTIAL LINES:

ONE Large pharma will leverage the experiences learned from managing R&D alliances to set up partnerships along other parts of the value chain, including marketing, distribution, public relations, customer relationship management, and regulatory compliance.

TWO As biotech companies grow larger and more confident in initiating and formulating partnerships, they will look to partner with organizations beyond the drug industry, including technology companies, academic institutes, and contract research organizations.

THREE Biotech companies will look to companies outside the industry to handle logistics, packaging, and other activities best handled by third-party providers. Like most industries, as biotech matures it will seek to partner with niche specialists.

SEVEN TIPS TO MASTERING THE ALLIANCE GAME

1. CODIFY THE MISSION AND STRATEGY up front. This requires consideration in three areas: culture, management, and organization.

2. UNDERSTAND THE DIFFERENCES between the partners' corporate cultures. This can be done by establishing four mechanisms at the outset: encourage openness and transparency among alliance members; establish a common purpose and goal; create a distinct culture for the partnership; and implement a set of clear performance metrics.

3. DISTRIBUTE UP-FRONT DOCUMENTATION of how management and staff changes are handled. By distributing this documentation, transitions can be handled smoothly and mitigate the impact on the alliance.

4. FORM A DEDICATED ALLIANCE MANAGEMENT TEAM. The team should cover three levels: alliance executives; alliance leaders; and alliance managers. Forming this team can help prevent the all-too-common mistake of diverting scientific resources from the goals of the project.

5. INVOLVE KEY MEMBERS FROM BOTH SIDES up front in strategy-development sessions. Building this decision-support infrastructure should provide management and staff with critical and timely information.

6. DEVELOP CONSISTENT METHODS for storing, viewing, and sharing data across the alliance, with the ultimate goal of adopting common industrywide standards. This makes communication and the sharing of data simple for the partners.

7. SHARE KNOWLEDGE SYSTEMATICALLY throughout the alliance life cycle and harvest it at the conclusion of the project. Systematic sharing and harvesting of knowledge can help improve the alliance's chance of success on an ongoing basis.

Source: IBM Healthcare and Life Sciences, Somers, N.Y. For more information, visit ibm.com/services/us.

THE PERFORMANCE STANDARDS FOR PARTNERING ON BOTH SIDES OF THE EQUATION ARE HIGHER. Companies have become more adept in developing alliance agreements, and this sophistication is extending across the value chain.

DR. JAMES CORTADA

lennium and Johnson & Johnson Pharmaceutical Research & Development LLC. Millennium is responsible for the commercialization of Velcade in the United States; Ortho Biotech and Janssen-Cilag are responsible for commercialization in Europe and most of the rest of the world. Janssen Pharmaceutical KK is responsible for Japan.

In March 2005, the company received approval to expand Velcade's indication to include the treatment of patients with multiple myeloma who have received at least one prior therapy. Velcade is now fully approved for treating relapsed multiple myeloma.

Leaders at smaller biotech companies point out, however, that it is only the larger biotech companies with late-stage products that are having a significant influence on negotiations.

"The perception about the position of strength of biotech relates to big pharma's need to get later-stage products to fill their pipelines," says Frank Armstrong, M.D., CEO of Bioaccelerate Inc. "I've spoken to development directors at the big companies, and they all ask if we have a Phase III primary-care product that would have peak sales in excess of $2 billion. Companies with these types of products are in a position of strength. For smaller companies, the issue remains finding the funding to pull products through clinical development."

David E. Thompson, VP of corporate strategy and business development at Eli Lilly & Co., agrees with that assessment.

"Tool companies and early-stage companies are having a great deal of difficulty in getting funding," he says. "These companies are chasing fewer dollars from the venture capital side and from the pharmaceutical companies. On the other hand, there is a lot of competition for biotech companies that have late-stage products that are in demand."

THE DEAL MAKERS

IBM's report found that biotech companies are more proactive than large pharmaceutical companies at forming alliances. Biotech respondents reported that they took the initiative 60% of the time in approaching pharma companies to discuss potential partnerships.

"Biotech companies are shopping around," Dr. Cortada says. "They need funding and they need prestigious alliances to make them more attractive to venture capitalists."

Dr. Cortada says another trend is that biotechnology companies are forming alliances with other biotech companies for some of the outsourcing tasks that they relied on big pharma to do, such as logistics, marketing, delivery, and manufacturing.

"There is a potential for all types of new companies to achieve dominance in the industry," he says. "In the future, some biotech companies may start to resemble large pharma companies."

ALLIANCE MANAGEMENT: A PROJECT MANAGEMENT PERSPECTIVE

AN ALLIANCE CAN BE A VALUE-ADDED STRATEGIC ACTIVITY THAT PROVIDES SEVERAL ADVANTAGES, including access to new technologies and/or capital, flexibility, lowered costs, and increased quality.

TIM NOFFKE

GUIDELINES FOR SUCCESS

DEVELOP A PLAN

- Basis for "business-side" contract requirements
- Contract provides the end; plan defines the means
- Communication and tracking tool
- A good plan does not necessarily equal MS Project

A GOOD PLAN INCLUDES

- Activities
- Durations
- Responsibilities/Accountabilities
- Processes that govern collaboration
- Resource requirements

EVALUATE PLAN

ENSURE AN UNDERSTANDING BY ALL INVOLVED

FORMALLY KICK OFF THE ENGAGEMENT

- Don't assume everyone was involved in contract development — ensure common focus
- A good kick-off meeting includes:
  - Introductions: roles and responsibilities
  - Review of contract terms
  - Presentation of historical/background data
  - Review and refinement of the plan
  - Visible endorsement from senior management sponsors

DEFINE THE COMMUNICATION PROCESS

- Ensure information systems are compatible
- Set communication expectations
  - Frequency
  - Forum
  - Participation/Requirements
- Identify primary contact person on both sides
- Be open and honest
- Acknowledge potential cultural/geographical obstacles

ACTIVELY MANAGE THE RELATIONSHIP

- Issues management
  - Issues arise and must be resolved real time
  - Attack the issue, not the person/organization
  - Issue-resolution approach:
    - Define decision-making authorities
    - Define criteria for assessing options
    - List options
    - Identify pros and cons
    - Prioritize options
    - Select the "best" option
    - Communicate the decision and rationale
    - Revise the plan and distribute a revised version
    - If required, revise the contract documents

CONTINUOUSLY COMMUNICATE

- Ensure no one is in a vacuum and all have the information they need to do the job
  - Face-to-face meetings
  - Teleconference meetings
  - One-on-one telephone calls
  - Informal discussions
  - E-mail, etc.

Source: Tim Noffke, PMP, VP, Life Sciences, Integrated Project Management Co., Burr Ridge, Ill. For more information, visit ipmcinc.com.

He says as biotech companies grow and gain enough scale, they could become specialists in a couple of disease areas that are very lucrative.

"As the interest in biologics increases, there are opportunities for companies to establish a body of knowledge that surpasses current standards," Dr. Cortada says. "This is very unusual for this industry; most of the major players have been around since the 1920s in one fashion or another."

Pharmaceutical companies are changing how they approach collaborations. Some are looking for opportunities earlier in the pipeline.

"Because there are fewer late-stage opportunities available, more of our focus is on earlier-stage opportunities," says Thomas Hofstaetter, Ph.D., senior VP of corporate business development at Wyeth Pharmaceuticals. "For the attractive late-stage products, there is heavy competition and the stakes go up. Earlier-stage opportunities are usually more affordable. Since

The Roche/ArQule Partnership

INDUSTRY EXPERTS SAY THE AGREEMENT BETWEEN ROCHE AND ARQULE IS A GOOD EXAMPLE OF THE NEW MODEL OF INTERDEPENDENCE OF COLLABORATIVE PARTNERS.

> OUR APPROACH TO ALLIANCE MANAGEMENT STARTS EVEN BEFORE DUE DILIGENCE. Our alliance directors meet with the executives from prospective company partners very early in the process. This allows both sides to establish a level of trust, which ultimately leads to bringing all the elements together to make the strategic partnerships work well.
>
> **CECE GATELY**

> THE CHALLENGE WAS HOW TO BLEND THE TWO COMPANIES' STRENGTHS to create value for both entities and increase the long-term value proposition, in other words the potential of the product.
>
> **ROBERT SILVERMAN**

In April 2004, Roche and ArQule began a partnership to discover and develop drug candidates targeting a new pathway to selectively kill cancer cells. The pathway influences the activation of a key cell death regulator called E2F. The activation of E2F plays a critical role in the programmed death of cancer cells, while leaving healthy cells unharmed. The partnership includes a compound in Phase I clinical development.

"We believe Roche had one of the early visions of an interdependent model," says Robert Silverman, director, global licenses, pharma partnering, at Roche. "We have a partnership with ArQule that is based on a relatively unique risk/value transfer dynamic."

Roche has an option to use ArQule's E2F program in the field of cancer therapy. Roche agreed to immediate funding of $15 million and significant financial support for ongoing research and development. ArQule's role is to advance drug candidates from early-stage development into Phase II trials. Roche may opt to license worldwide rights for the development and commercialization of products resulting from this collaboration by paying an option fee. Assuming the successful development and commercialization of a compound under the program, ArQule could receive up to $276 million in payments, plus royalties. Additionally, ArQule has the option to copromote products in the United States.

Roche depends on ArQule for innovation, and ArQule depends on Roche for development expertise, says Cece Gately, director, global alliances, pharma partnering, at Roche.

"ArQule has a great knowledge base in chemistry," she says. "We believe the company brings a real strength in the quality and depth of its research efforts to the partnership. ArQule's researchers are very innovative and have big chemistry strength. They can come up with new molecules to back up the company's own pipeline. ArQule acknowledges that it doesn't have global development, regulatory, or marketing expertise, some of the strengths of a big pharmaceutical company; this is where Roche comes in."

Mr. Silverman says in developing this model both companies had to think outside the traditional partnership agreement structure.

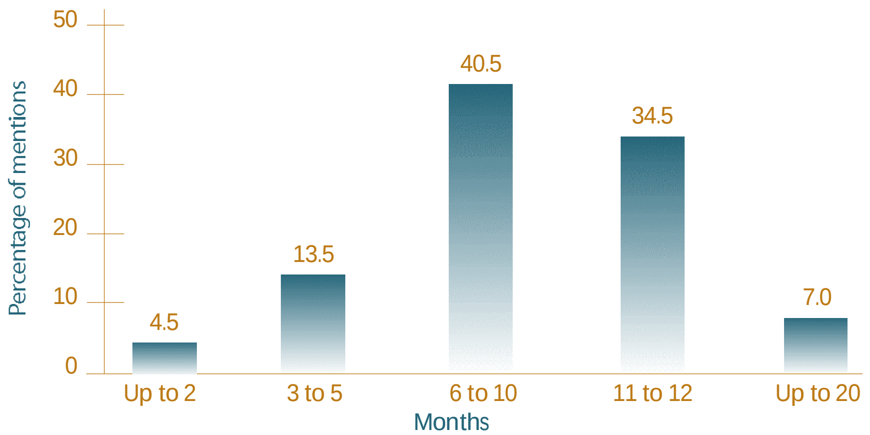
"The challenge was how to blend the two companies' strengths to create value for both entities and increase the long-term value proposition, in other words the potential of the product," he says. "The result is an interdependent structure. Roche depends on ArQule's strength in focus, and ArQule depends on Roche for its strength and breadth."

Roche has a thorough risk-assessment and due-diligence process that it undertakes for all of its partnerships.

"We very carefully assess the management and leadership of the other companies," Mr. Silverman says. "We look for partners that we believe have vision and credibility. For Roche, partnerships are about creating long-term relationships."

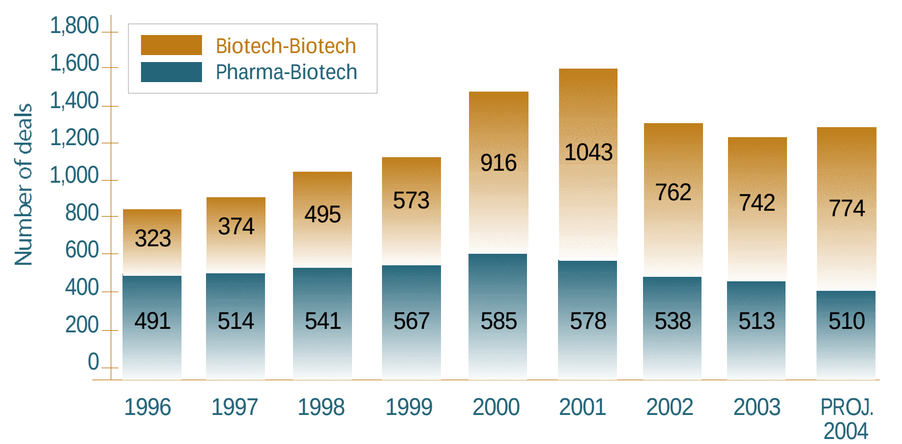
KEY TRENDS IN THE STRATEGIC BIOPARTNERING ARENA

TIME-TO-DEAL



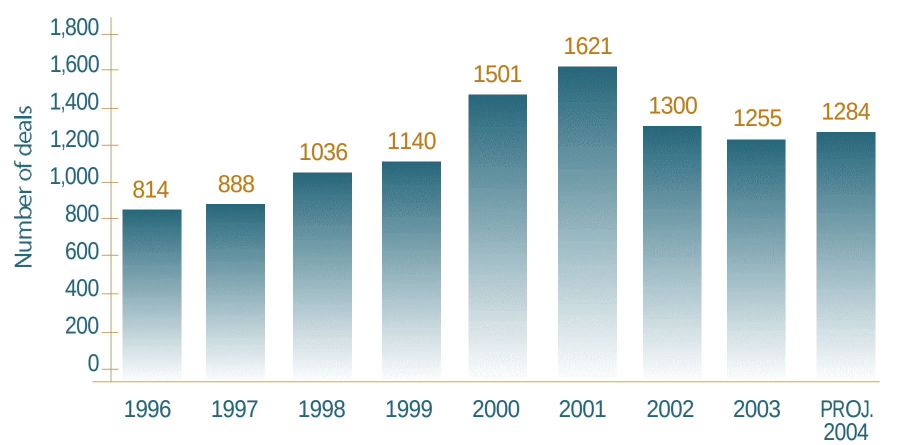
Note: The 2004 survey defined "time-to-deal" as the time of first contact between prospective partners to when a contractual agreement is signed by both parties.

MULTINATIONAL PHARMA COMPANIES NO LONGER DOMINATE PARTNERING PROSPECTS



Note: For this analysis, a drug company was classified as "pharma" if it existed before the advent of the biotech industry.

THE RATE OF NEW DEALS



Note: These totals encompass all types of alliances, including mergers and acquisitions.

Source: IBM BioPartnering 2004 Survey, IBM Business Consulting Services, Somers, N.Y.

MORE DEALS, MORE QUICKLY, BUT NOT QUICKLY ENOUGH

THE FIRST MAJOR FINDING OF THE BIOPARTNERING 2004 SURVEY is that, while the number of alliance deals is growing, deals are not being signed as quickly as they could be.

The survey found that average time-to-deal has improved by one-third during the past five years to 10.7 months (see chart to the left). Analysis by IBM indicates, however, that even with recent strides, time-to-deal is still too lengthy.

From the perspective of biotechs, up-front payments are a critical component of alliance deals, with 63% of alliances including them, according to the 2004 survey. But having to wait months on end for an up-front payment can erode whatever time advantage a biotech may have enjoyed at the start. Especially for biotech startups, payments can provide a critical "halo effect" that reassures venture capitalists and other shareholders and keeps the investment dollars flowing. In some cases, the timing of a payment can actually make or break the company.

The number of new deals doubled between 1996 and 2001, from 814 to 1,621. Since then, the number of deals has stabilized to about 1,300 per year. This pattern in part reflects the challenges the global economy experienced in 2001.

THE CENTER OF GRAVITY SHIFTS FROM PHARMA TO BIOTECH

THE SECOND MAJOR FINDING OF THE BIOPARTNERING 2004 SURVEY was biotechs that survived speculative excesses of the 1990s have matured into sophisticated deal-makers. While still key players, multinational pharma companies no longer dominate in the biotech alliance game. Since 1999, deals between biotech companies have outnumbered biotech-pharma deals, and the gap is set to widen.

The number of biotech-biotech deals more than tripled between 1996 and 2001, while the number of biotech-pharma deals grew less than 20%. Between 2001 and 2003, both types of deals declined as a result of marketplace setbacks. Even so, the number of biotech-biotech deals signed in 2003 was more than double the number signed in 1996. The same cannot be said of the number of biotech-pharma deals, which was only slightly higher in 2003 than in 1996. In 2004, the number of biotech-pharma deals is expected to continue to decline.

As this trend suggests, the biotech industry has matured to the point that larger biotechs are able to support smaller biotechs in alliance scenarios. Today, "big biotech" is beginning to acquire some of the characteristics of big pharma (while retaining many desirable operational habits of biotechs, such as agility, responsiveness, and flexibility). In some cases, senior pharma executives take biotech positions late in their careers, further adding to the pool of experience biotechs can draw from when they form alliances.

BIOTECH COMPANIES ARE FINDING THAT THERE IS AMPLE MONEY AVAILABLE IN PUBLIC MARKETS and through private venture capital. As a result, they are less likely to license away the crown jewels than they were 10 to 15 years ago.

TRACY LEFTEROFF

we know what our needs are, we can find more potential early-stage candidates."

For obvious reasons, early-stage deals are riskier for pharma companies.

"Our basic philosophy for partnering is to create a win-win situation so that both parties benefit from the collaboration," Dr. Hofstaetter says. "This includes sharing risk and reward; if the risk is higher, we would expect the terms to reflect this."

Lilly is another pharmaceutical company looking at more early-stage product alliances.

"It's important to look outside the obvious," Mr. Thompson says. "We have partnerships throughout the entire value chain — from collaborations at the earliest discovery technology stages, to target validations, target identification, through products that are on the market. We set up an alliance management group long ago because partnering has been a fundamental piece of our strategy since the mid-1990s. This is important because we know we can't do it all."

ENSURING SUCCESS

The IBM report indicates that more than half of the alliances between biotech and pharma companies are not effective, and 85% of alliance failures can be attributed to causes that can be managed. Survey respondents identified several deal-making pitfalls that can be avoided: inadequate due diligence that can leave partners overestimating the market potential of deals; imbalanced negotiations that can result in unequal benefits and poorly defined roles for partner companies; and a lack of care in contract wording.

Better alliance-management practices could salvage a potential $2.7 billion annually, according to IBM.

Mr. Thompson says it is important to bring alliance management executives into the negotiation process.

"The role of our alliance group is relationship management," he says. "We try to get the right 'owners' involved so they understand the give-and-take of the transaction. It's important they understand not only the words on the paper but the spirit behind the transaction."

Dr. Hofstaetter says it's also important to spend sufficient time to understand what the real needs and goals are of each partner.

"In my experience, one of the main reasons alliances don't perform well is that there isn't a good alignment in terms of respective goals and interests," he says. "This gap is usually reflected in the contract and later in the implementation phase."

Dr. Redpath says another challenge is the contract itself, which needs to be clearer.

"Many companies focus more on what to do if things do happen and less on what to do if things don't happen," he says. "Termination scenarios and dispute resolutions are important; the key to a good licensing deal is defining what to do when things don't go according to plan." ✦

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

Experts on this topic

FRANK ARMSTRONG, M.D. CEO, Bioaccelerate Inc., New York; Bioaccelerate acquires and develops pharmaceutical compounds that have substantial medical and commercial value. For more information, visit bioaccelerate.com.

JAMES W. CORTADA, PH.D. Team Leader, IBM Institute for Business Value, IBM Business Consulting Services, Somers, N.Y.; IBM Institute for Business Value develops strategic insights around critical industry-specific and cross-industry issues. For more information, visit ibm.com/services/us.

CECE GATELY. Director, Global Alliances, Pharma Partnering, Roche, Nutley, N.J.; Roche is a research-oriented healthcare group with core businesses in pharmaceuticals and diagnostics. For more information, visit rocheusa.com.

THOMAS HOFSTAETTER, PH.D. Senior VP, Corporate Business Development, Wyeth Pharmaceuticals, Madison, N.J.; Wyeth has products in the areas of women's healthcare, cardiovascular, central nervous system, inflammation, transplantation, hemophilia, oncology, vaccines, and nutritional products. For more information, visit wyeth.com.

TRACY LEFTEROFF. Global Managing Partner, Life-Sciences Industry Services, PricewaterhouseCoopers, Boston; PWC provides industry-focused assurance, tax, and advisory services for public and private clients. For more information, visit pwc.com.

TIM NOFFKE. PMP, VP, Life Sciences, Integrated Project Management Co., Burr Ridge, Ill.; IPM provides project management leadership to chemical and petroleum, consumer products, food and beverage, healthcare facilities, and life-sciences industries. For more information, visit ipmcinc.com.

ANNA PROTOPAPAS. VP of Corporate Development, Millennium Pharmaceuticals Inc., Cambridge, Mass.; Millennium is a biopharmaceutical company with research, development, and commercialization activities focused in three therapeutic areas: oncology, cardiovascular, and inflammation. For more information, visit millennium.com.

KEITH REDPATH, PH.D. Head of the Life Sciences Research Team, Wood Mackenzie, Boston; Wood Mackenzie provides a wide range of consulting services and research products to the energy and life-sciences industries. For more information, visit woodmac.com.

ROBERT SILVERMAN. Director, Global Licenses, Pharma Partnering, Roche, Nutley, N.J.; Roche is a research-oriented healthcare group with core businesses in pharmaceuticals and diagnostics. For more information, visit rocheusa.com.

DAVID E. THOMPSON. VP, Corporate Strategy and Business Development, Eli Lilly & Co., Indianapolis; Lilly is developing a growing portfolio of first-in-class and best-in-class pharmaceutical products. For more