

Biotech Responds to Dramatic Changes to Innovate in 2010 and Beyond



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INTRODUCTION



James C. Greenwood
BIO President & CEO



Robbi Lycett
Vice President,
Conventions & Conferences

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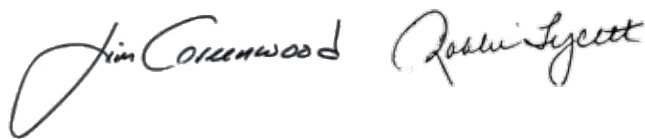
We are pleased to provide you with a series of articles we produced with our media partners in 2009. In a year with many marketplace changes, the content is focused on helping you adapt to the ever-evolving business climate and move forward in 2010.

If you haven't already registered, please consider joining us at the 2010 BIO International Convention in Chicago, May 3-6, 2010. The convention addresses your business challenges and delivers unprecedented partnering opportunities.

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Partners in Survival

Biotech executives have responded to the dramatic changes in the world around them by forging strategic alliances.

By Peter Winter

While it may be several months before the biotech industry starts on its road to recovery, many companies are turning to partnerships in the tight fiscal climate that they currently find themselves in. Partnering is proving to be an effective strategy that can keep cash strapped biotech companies functioning and solvent through the economic crisis. Given the demonstrated successes of partnering over these past few years, the positive dynamic upturn is likely to continue. This is reflected in the fact that a massive \$12.7 billion in reported total deal values was raised by U.S. biotech firms through partnering in the first half of 2009. This amount was up almost 76 percent over the comparable period a year earlier according to data compiled by *The Burrill Report*.

Partnering aspirations are not only top-of-mind among biotech executives in the United States. In Canada, PricewaterhouseCoopers' "Canadian Life Sciences Industry Forecast 2009", completed in collaboration with Canadian industry association BIOTECCanada, found that almost one third of the executives surveyed expected their funding requirements would come from strategic partners. Other major sources included private equity funds (20 percent), venture capitalists (19 percent) and angel investors (18 percent). "With the public markets challenging, industry is looking for strategic partnerships and private equity funds to at least partially fill the gap and enable the continued development of lead programs," says Peter Brenders, President and CEO of BIOTECCanada.

Biotech companies are tackling their funding crises on two fronts: they are cutting costs to reduce their burn rate and seeking to access capital from external sources. Typical of this trend among emerging biotech companies is Boulder, Colorado-based Array BioPharma, which in January announced plans to accelerate its own partnering initiatives and scale back discovery research spending over the next 24 months to help ensure sustainable growth through uncertain capital market conditions. During 2009, Array expects to reduce net cash used in operating activities from approximately \$30 million per quarter to \$20 million per quarter, before new partner or milestone payments.

"We are putting in place multiple measures to allow our most promising programs in cancer, inflammation and diabetes to rapidly advance in clinical development," Robert Conway, CEO of Array BioPharma, said at the time. "It is important to conserve our



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cash resources during these difficult times for the financial markets and focus our efforts on advancing clinical programs through proof-of-concept to maximize their value.”

Mention strategic alliance partner to any biotech executive a few years ago and their thoughts would immediately go to Big Pharma. It was the well tried “road to success.” The strategy was to develop a product through to mid-stage clinical trials and then attract a pharma company to help with development the rest of the way. However, in these stressed economic times, this strategy has been turned on its head as the partner can now be any company that can provide a source of cash and support for early- or late-stage drug development.

For example, small-cap Transcept Pharmaceuticals struck a \$145 million commercialization agreement with privately-held Purdue Pharma for its insomnia drug Intermezzo. The deal came three months ahead of the date the FDA was expected to rule on its application to begin marketing the drug. Transcept granted Purdue an exclusive license to market, sell and distribute Intermezzo in the United States and the right to negotiate for the commercialization of the product in Canada and Mexico. Transcept retained an option to co-promote Intermezzo to psychiatrists in the United States and retained rights to commercialize the drug in the rest of the world. Besides an upfront cash payment of \$25 million and an additional payment of up to \$30 million based on the timing of an FDA approval, Transcept will be eligible to receive up to an additional \$90 million in future milestones and royalties on sales.

Transcept is new to the public markets. It gained a Nasdaq stock market listing through a reverse merger with Novacea in February. Intermezzo has met its primary endpoints in three late-stage clinical studies. If approved, Intermezzo would be the first drug approved for patients who wake up in the middle of the night and have trouble falling back to sleep.

Two other small-cap biotechs Facet Biotech and Trubion Pharmaceuticals also recently hooked up, signing a worldwide collaboration agreement to jointly develop and commercialize TRU-016, a product candidate in early-stage clinical development for chronic lymphocytic leukemia. Trubion will receive an upfront payment of \$20 million and may receive up to \$176.5 million in additional contingent payments upon the achievement of certain development, regulatory and sales milestones. The companies will share equally the costs of all development, commercialization and promotional activities and all global operating profits. In addition, Facet will purchase 2.2 million shares of newly issued Trubion common stock for an aggregate purchase price of \$10 million.

Pharma still remains an important player in the partnership mating game. However, since the financial meltdown, the relationship between pharmaceutical and biotechnology companies has changed dramatically. With biotechs facing a funding crisis and eroding market values, pharmaceutical companies are now more likely to prefer acquiring biotech targets out right, rather than navigating the road of complex



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licensing agreements. Nevertheless, partnership deals between biotech and Big Pharma, both big and small, continue to get done.

Boston startup MSM Protein Technologies is leveraging its proprietary suite of tools for drug discovery of functional antibodies and proteins against multi-spanning membrane proteins through two partnership deals. One with Merck Serono to create antibody based products targeted to G-protein coupled receptors and other possible targets in the cell membrane. The other with Debiopharm Group, a Swiss-based global biopharmaceutical group of companies for the development and commercialization of Debio 0929, an antibody targeting a G protein-coupled receptor, to be developed into a new oncology therapeutic drug.

In addition, small biotech Opexa Therapeutics, a company developing a novel T-cell immunotherapy for multiple sclerosis, landed \$4 million upfront and a potential for \$50 million in milestones through a collaboration with Novartis to develop Opexa's preclinical stem cell technology.

In today's uncertain times, partnering is providing an important funding surrogate role for biotechs in the absence of an IPO window and as VCs remain cautious with their investment dollars. Few biotechs can take the risk of not exploring the opportunities offered by partnering to find capital or product candidates elsewhere in the world. ■



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The Year that Wasn't

Merger & acquisition activity slowed in the second quarter, but it's viewed as a temporary lull as plenty of companies still look to be acquired.

By Daniel S. Levine

Last year started off with an M&A bang as a series of mega mergers seemed to set the stage for 2009 to be defined by robust M&A activity. And why not? Big Pharma was racing toward a cliff with its biggest blockbusters approaching patent expiration. These companies had plenty of cash to fuel a shopping spree. On the other side sat plenty of financially strained biotechs that no matter how promising their pipelines were, found it difficult to raise money. And with an IPO window nailed shut, private companies looking for an exit had little choice but to turn to M&A. But while in the first half of 2009, M&A activity raced in like a lion, in the second quarter it went out like a lamb.

There were of course the show-stopping multibillion deals of Pfizer-Wyeth, Merck-Schering-Plough, and Roche-Genentech. But in the second quarter of 2009 the number of M&A transactions decreased by about 71 percent compared to the same period a year ago, according to Burrill & Company. GlaxoSmithKline's \$3.6 billion purchase of Stiefel Laboratories was the only marquee transaction during the quarter.

"It's been a tough financing environment and you can't ignore that when you look at M&A, and the expectations for such transactions," commented George Milstein, managing director of healthcare mergers and acquisitions for the investment bank Wedbush PacGrow, who said it was easy for people to focus on the large deals and conclude that we're on target for the biggest M&A year in history. While that may well be true from a dollar amount standpoint, he says it doesn't have much to do with mid-sized biotech companies.

"Most folks predicted that the weak financing environment would force more companies to sell – both public and private. What you start running into is the fact that there are not an insignificant number of companies for sale, or that are trying to figure out how they are going to fund their next program no matter how good the data are," he says. "There are only a limited number of buyers."

The drop in activity may have been a bit unexpected for many, but M&A watchers like Milstein say it's not surprising because in part it's due to the



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fact that some of the most likely acquirers are busy trying to digest the large acquisitions they have bitten off already. Others, though, say it also reflects the depressed values on biotech stocks experienced earlier in the year. With prices down, many companies explored their options for how to realize their best value.

John McCamant, editor of the Medical Technology Stock Letter, says that the value of the smaller biotechs fell so low that it would not have been within board members' fiduciary duty to sell the companies. He points to the recent \$2.4 billion acquisition by Bristol-Myers Squibb of Medarex. The \$16 a share bid represented a 90 percent premium over the closing price of the stock when the deal was announced in July. But the stock had traded roughly between \$3 and \$9 during the previous year. "Suppose someone gave them a 100 percent premium at \$3 or \$4. That would not have been a good deal for the shareholders," he says. "As we get better valuations, it's starting to step up."

McCamant thinks the Medarex deal reflects the types of acquisitions that Big Pharma companies will seek out — buying entire companies to get access to a platform rather than placing a bet on a single late-stage candidate. Medarex offered BMS access to technology for human monoclonal antibodies that McCamant describes as dominant, well-protected intellectual property, a pipeline, and biotech expertise that includes manufacturing.

But for many smaller companies, the pressure remains to find ways to tread water until they can consummate a deal or find new sources of financing. Matthew Hudes, U.S. managing principal for biotechnology for Deloitte says what hasn't materialized has been the fire sales many expected. "We're really not seeing them, at least from an M&A perspective," he says. "What we are seeing is the outlicensing of valuable assets. We're seeing a lot more licensing of, if not the crown jewels, at least the valuable jewels."

Wedbush PacGrow's Milstein says he expects to see a pick up in activity as we move forward, but that the best opportunities for companies seeking buyers will likely not be the usual suspects. Instead, he says that many of the companies would be wise to look at some of what he calls the "emerging powerhouses." This includes well-heeled specialty pharmaceutical companies, large-cap biotechs, and companies that have traditionally been thought of as generic makers. "These companies are in a position to leverage their R&D and sales infrastructure and they are going to do it," he says. "There are some really interesting avenues for small- and mid-sized companies and to focus just on the same ten people they've been calling for the last ten years is just not the way to do it."



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M&A deals take time. Buyers need to understand exactly what they are buying and want to be comfortable with whomever they may be marrying their company's future. The trick for many companies up for sale right now is to make sure they keep their operations afloat and move forward. Some will be racing against dwindling resources that may run out before they are able to secure a buyer or find near-term financing. No doubt, there will be those that do not make it and will be forced to liquidate. But there is plenty of talking and tire-kicking going on right now and reason to expect M&A activity will heat up again before 2009 ends. ■



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Big Pharma's move toward targeted therapeutics is fueling dealmaking between drug and diagnostics companies.

By Marie Daghlian

The promise of personalized medicine—therapeutics tailored to treat specific patient populations—has emerged as a key driver in drug development. Rather than reach for mass market blockbusters, pharmaceutical and biotech companies are focusing on therapies to treat patient populations with specific subtypes of a disease. As the importance of having a diagnostic paired to such therapeutics grows, so too will the number of mergers, acquisitions, and partnerships built around companion diagnostics according to a new PricewaterhouseCoopers (PwC) report.

“We think that diagnostics is the tip of the spear in personalized medicine and this trend will continue as there is more proof of clinical utility,” said Gerry McDougall, Principal, Healthcare Advisory Services, and one of the authors of the report “Diagnostics 2009: Moving toward personalized medicine.”

The report noted that 2007 was an exceptional year for M&A in the in vitro diagnostics sector with 84 deals with a disclosed value of \$26.5 billion. M&A deal flow dropped in 2008 to 51 deals with a disclosed value of \$1.7 billion. And although the economy could be blamed for some of this downturn, in part it was due to the simple fact that the industry had to digest the record number of deals from the previous year. Partnering and licensing activity also peaked in 2007 with 27 announced in-licensing deals, compared to 18 such deals in 2008.

In spite of this slowed pace of deals, the PwC report expects that the growth of personalized medicine will drive pharmaceutical/diagnostic deal activity in the years to come. According to research and consulting firm MarketsandMarkets, the global biomarker market is estimated to grow at a compounded annual growth rate of 19.7 percent in the next five years to reach \$20.5 billion by 2014.

While the PwC report argues there has yet to be significant deal flow between the pharmaceutical and diagnostics industries, several factors are driving pharma companies to increasingly rely on in vitro diagnostics, and specifically on companion diagnostics. Companion diagnostics, in the broadest sense, that can help identify an individual patient's likelihood of benefiting from a particular therapeutic. They can range from tests to identify a biomarker to ones that identify a specific genetic variant.



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Driving personalized medicine deals is the increased use of diagnostics to identify the right group of patients in an effort to cut drug development costs. By using these tests to identify patients most likely to benefit from a therapy, drugmakers hope to reduce the size and increase the success of clinical trials. They also hope such an approach will help drugs in development pass muster with an increasingly risk averse FDA.

The benefits can be seen throughout the development cycle. “If you can select patients that are more likely to respond to your therapeutic agent than patients at random, or unselected patients, then you are more likely to have a successful clinical trial,” says Joe McCracken, Genentech’s vice president of business development. “It requires fewer patients. In addition, I think the FDA is more comfortable when they look at the risk/benefit profile for the drug.”

Companion diagnostics are essential to the execution of the business strategy for Genentech. McCracken says that diagnostic collaborations are not their primary focus, but when they seek to in-license a product, they want a diagnostic concept to be a part of the collaboration. “At Genentech, the concept of a diagnostic and a therapeutic are so integrated that I have difficulty really articulating a strategy for either of those as separate strategies,” he says. “They really are the same for us.”

In August, Genentech signed a deal with Danish diagnostic company Dako to collaborate on the regulatory submission of Dako’s HER2 tests as companion diagnostics for Herceptin in patients with advanced HER2 stomach cancer. McCracken thinks we are still in the early stages of embracing personalized medicine but he sees it as a trend that is likely to get stronger. Right now there are only a handful of therapies that require a companion diagnostic as part of the prescription. “I know that there are a number of research-stage or development-stage product concepts that aren’t approved yet, but I think ultimately will be approved,” he noted. “In the future, as companies increasingly focus on specialty products, this will be an important growing trend.”

The PwC report noted that out of 18 in-licensing deals announced by major pharmaceutical companies in 2008, eight were focused on technologies for the early detection of cancer. In fact, pharmaceutical companies’ focus on oncology is a good harbinger of deals to come. Cancer drugs are among the most expensive therapeutics and have become big revenue producers for the industry. In 2008, cancer drugs accounted for 20 of the 126 drugs with sales over \$1 billion, according to trade magazine Med Ad News. Cancer is also a complicated disease that arguably covers many disease types. With advances in genomics and proteomics, it has become easier to characterize individual disease subtypes to determine the effectiveness of a particular therapeutic.

It also has become imperative from a financial perspective as companies seek to stretch their drug development dollars by improving their efficiency and payors seek to reign in healthcare costs by not paying for therapies that won’t provide benefit to specific patients. A good example of the pharma trend is Pfizer’s recent deal with



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Abbott to develop a companion diagnostic to determine a patient's genetic status before a planned late-stage clinical trial for its non-small cell lung cancer compound. Only about five percent of lung cancer patients will qualify for the trial.

Stephen Little, CEO of the Manchester, United Kingdom-based companion diagnostic company DxS, thinks the future looks bright for striking personalized medicine deals because many parties can benefit. "One of the potential beneficiaries is the pharmaceutical industry," he says. "An important change that we've noticed is that drug companies have moved from the position of really being quite resistant to the idea of using a companion diagnostic to embracing it."

Deal pace has picked up momentum in the second and third quarter of 2009, with nine licensing deals and two major M&A transactions announced so far this year. DxS has been busy. The company reached a deal with AstraZeneca in early August to develop its EGFR mutation kit as a companion diagnostic for AstraZeneca's Iressa to target the therapy to the less than one-fifth of patients that can benefit from the lung cancer treatment. DxS is also working with German pharmaceutical company Boehringer Ingelheim to develop its EGFR test as a companion diagnostic for a non-small cell lung cancer therapy before the start of late-stage clinical trials.

The ideal situation—collaborating before the drug is approved. "We are starting to see a trend for drug companies to start thinking about the companion diagnostic earlier in their development program," says Little. It means that the alignment of the Rx/Dx development can be better coordinated. The company has also signed agreements with Amgen and Bristol-Myers Squibb to provide an EGFR assay to identify the K-RAS oncogene in colon cancer tumors.

Little says companies are knocking on his door to do companion diagnostic deals, unlike a few years ago when the concept was not well established. He definitely sees an uptick in M&A activity and partnerships built around companion diagnostics. "I think a lot of the concerns that drug companies had about just how would a companion diagnostic strategy work have been allayed, because we have seen it working in practice," he says. "In light of that, we should expect that more deals will become available as drug companies decide to pursue this route—particularly in oncology. I think the jury is still out about other areas of medicine." ■



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