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Drug discovery paradigm shift

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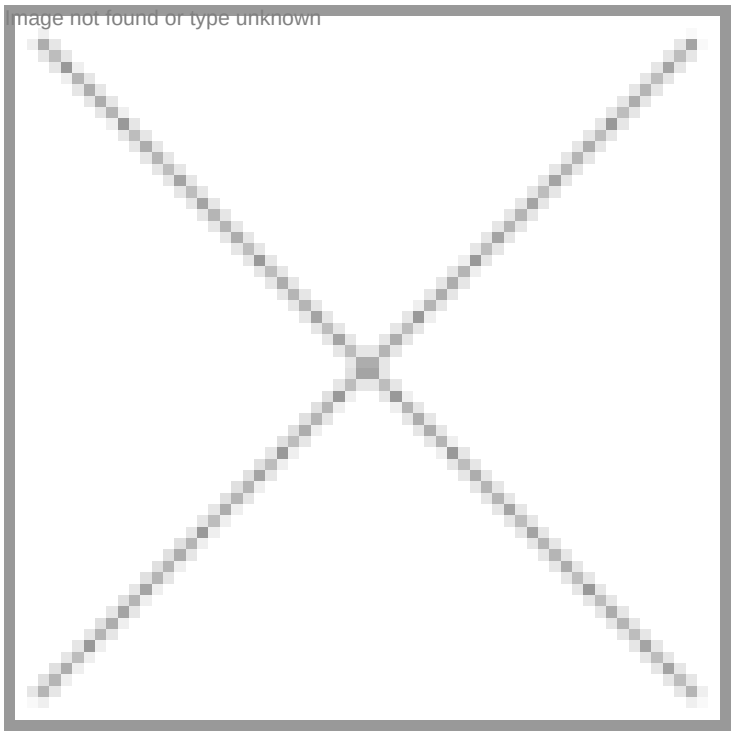
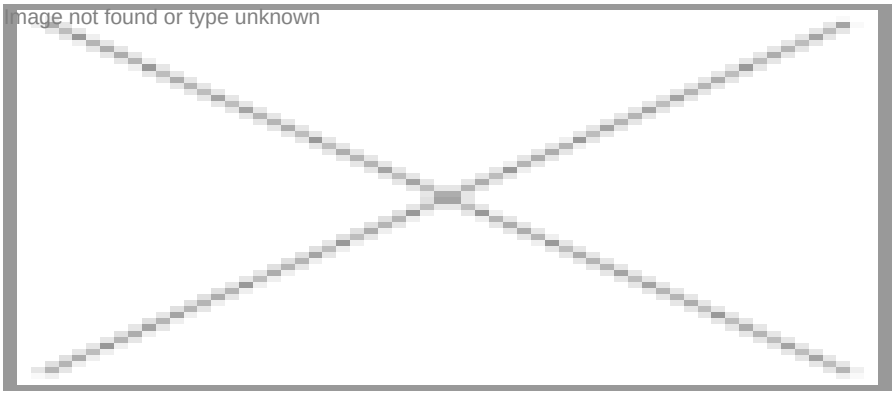


Drug discovery paradigm shift

A convergence between the pharma and biotech sector will gradually see both parties leveraging their strengths in drug development, commercialization, discovery and manufacturing capabilities thus delivering innovation and changing the whole landscape of M&A deals.

Global pharmaceutical companies have been swimming in troubled waters for quite some time but the good news is that they are now on the proactive mode.

Big pharma's acquisition spree started making big news since 2008. In January 2009, Pfizer acquired biotech big-wig Wyeth for $68 billion, followed by Roche ending its long drawn hostile battle with Genentech by buying the remaining 44 percent stake, thus acquiring the latter for $46.8 billion. This was followed by Merck's announcement in March to acquire Schering Plough for $41.1 billion. Other big deals include: El Lilly's purchase of ImClone Systems last year, Japanese giant, Takeda Pharmaceutical's acquisition of Millennium Pharmaceuticals and Cephalon's takeover of Australia's Arana Therapeutics.



Convergence is the trend

Analysts claim that convergence between pharma and biotech companies is not a new trend and will continue to do so. Sujay Shetty, associate director, Pharma Life Sciences Advisory, PricewaterhouseCoopers (PwC), says, “From a global perspective, these big acquisitions have been taking place for the obvious reasons like the R&D pipeline drying up, and at the same time, biotech companies are either discovering a new molecule or a drug platform which could help replenish that pipeline. Deals like the Takeda-Millennium, ImClone-El lilly, Roche-Genentech will continue as long as big pharma sees the need to augment its pipeline which is not created in-house.”

Patent expirations will open the way for a fierce generic competition. “A lot of drugs are going to be off patent in future and will face fierce competition from the generic companies, thus will marginally reduce the revenue of the pharma companies. Increasing issues on drug safety norms delaying entry of new drugs into the market due to the stringent regulations in the clinical trials are some of the other reasons for pharma and biotech companies coming together,” says Bibhuti Bhusan Kar, program manager, South Asia & Middle East, Healthcare-–Pharmaceuticals & Biotechnology, Frost & Sullivan. Hence, industry experts claim that convergence between the two will drive the wheels of the much needed innovation for the industry. It is a healthy market which will be the apt solution for big pharma’s reeling woes.

A PwC report on ‘Lifting big pharmas prospects with biologics’ , mentions that it will primarily be the biologics sector which will drive the M&A activity with protein-based therapeutics, MAbs and vaccines being hailed as promising sectors for growth. The same report also goes on to mention that in 2008, the therapeutic monoclonal antibodies sub-sector drew increased investment of $640 million in 46 deals, up from $477 million with 41 deals in 2007. Four of the top 10 human biotech deals in 2008, were companies focusing on therapeutic MAbs. It is also estimated that the market for MAbs is estimated to grow at a CAGR of 16.9 percent between 2006-12. Vaccines also drew in a considerable amount of investment of $494 million from 31 deals in 2008.

“In many therapeutic areas like CNS, Alzheimer’s and diabetes, we have seen that further meaningful innovation is not happening. Companies have been shifting their focus now on the root cause of any disease and understand the corrective measures to be taken more at the genetic level. Hence, a convergence between biotech and pharma will result in newer ways of finding curative therapies than the traditional synthetic ways,” opines Nair.

Moreover, maintaining an almost perfect balance between innovation on one hand and cost-efficiency on the other, it becomes the center of attention for strategy teams. Shetty mentions, “Pharma is on the lookout for new pipeline drugs. They have typically addressed that and are going out and buying companies. Companies are now saying that by 2012, they are to lose revenues and their scientists are not coming up with anything innovative. Therefore, buying a biotech company is the best option to keep those revenues flowing in.”

“As far as cost-reduction is concerned, pharma has got a huge infrastructure for R&D. Now there is a hope for them to do it more efficiently, not just in R&D but also for the ground level and fast-end clinical works,” he adds. To keep their business up and running, companies are now drawing up biological strategies which also include tapping emerging markets. The nature of competition is such that one day a company’s revenue might be $10 billion and with patent expiry, it is zero. “This does not happen in any industry. So the challenge is always on the innovation part of it, and cost comes after that,” observes Shetty.

The recent trend of convergence has thus changed the rules and landscape for M&A deals in the life sciences industry.

Sudeep Krishna, co-lead, Healthcare and Life sciences, Deloitte India, says, “The recent convergence trend has changedthe rules of M&A activities, in the sense that traditionally we’ve seen that a pharma company acquires a biotech company having one or two blockbuster drugs with the deal around Rs 100-200 crore. Now, we see them acquiring big biotech companies having a whole pipeline of promising targets because big pharma has the money. The interesting aspect we’ve to look out for is the manner in which they integrate the entities especially the talent pool from both the entities.”

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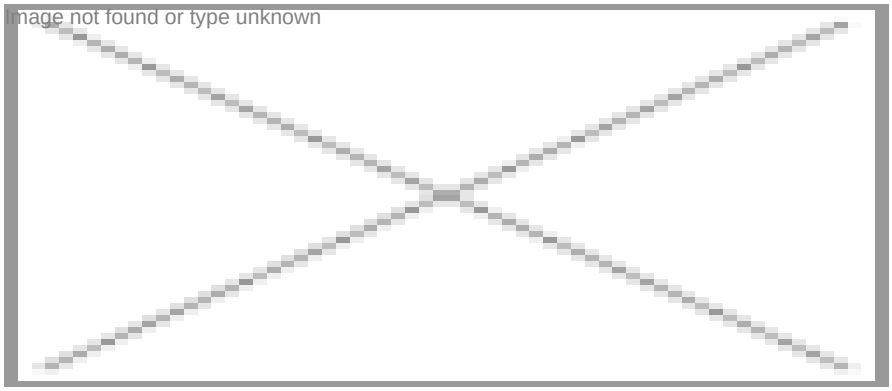


Impact of convergence

Drug innovation: With the convergence, the industry will now see a gradual blurring of boundaries between the biotech and pharma sectors. Such a convergence will open up avenues in the drug innovation process, the most obvious reason being that biotech companies whose forte has been innovation will replenish the drying up pipeline of pharma companies. “I think that drug innovation will go through a positive transformation. Now the cure will be much more holistic,” says Nair. Genentech for example, has cutting-edge products in both biotechnology and cancer medicines – with blockbusters

Avastin, which churned a revenue of around $2 billion last year and Herceptin, an extensive portfolio of new drugs.

Over the past one year, the number of FDA approvals for biologics has seen a gradual rise. For example, in 2008, there were 20 new molecular entity (NME) and four new biologics as compared to 16 NMEs and two biologics in 2007. Says Sanjay Singh, associate director, corporate finance, KPMG, “Biotech will aid significantly in drug discovery research especially in target identification, and lead generation and optimization activities.”

Moreover, big pharma companies are cash-rich companies. Hence, investing in expensive assets such as biologics is a risk they’re willing to take, considering the returns they’ll reap at the end. “With biotech companies focusing on molecular biology and genetic engineering approaches, and with pharma companies being the lavish spender in R&D for drugs with basic chemistry one can expect a larger success rate in terms of output from the biotech drug development rather than pharma,” says Kar.

The whole process of drug innovation is an expensive one which does require a continuous inflow of monetary funds, and convergence will be a solution to the problem.

Licensing deals: Typically, a biotech company is always on the lookout for revenue churning options. So licensing deals are the answer to the question wherein a biotech company can expect an inflow of cash returns in the form of upfront payments, milestone payments and royalties. Opines Krishna, “Licensing deals between pharma and biotech companies have been happening for a long time and will continue to do so. In fact, I would say that it was these licensing deals which was a stepping stone for a convergence of such a kind.” “Biotech companies had to out-license their molecules because of their limited market access, and pharma companies in-licensed molecules from biotech companies which looked promising. Later pharma companies went a step further and thought why not go in for an acquisition of these entities,” he adds.

An important fact to bear in mind is that big pharma’s primary capability is commercialization while biotech strength lies in discovery and manufacturing. “Big pharma has much deeper pockets. In the present global economic environment, biotech, which has traditionally been a beneficiary of venture capital (VC) and government funding, will have challenge in keeping the fund flow. Hence, a natural consequence of this will be licensing deals which focuses on leveraging each others strength for the best outcome,” adds Nair.

Outsourcing: Outsourcing projects on the other hand will either see a status quo or a gradual increase but not drop. Opines Singh, “It’ll lead to outsourcing of high-end preclinical research to Indian companies, though it’ll be a slow and gradual process as Indian companies will need to demonstrate their skill and knowledge base in high-end preclinical research areas.” VCs will also have a pivotal role to play. The VC market has supported the growth of the outsourcing market due to the fact that there’s a significant risk involved in bringing a drug to the market.

Manufacturing: Manufacturing is another area which will see a positive transformation with biotech being a catalyst in the transformation. The dynamics of biotech manufacturing is different from pharma manufacturing, hence, the former will remain as a separate unit post-integration. “A convergence will lead to a need to invest in specialized, high-end fermentation and purification units,” says Singh.

At a closer look, a pharma company will reap more benefits than its biotech counterpart. “If you look at the top 10 pharma companies, they have all made biotech investments but their manufacturing capabilities are limited. Hence, a biotech manufacturing facility will be an additional and useful asset to a pharma company,” adds Krishna.

Biosimilars: With biosimilars being the buzz word, and some movement happening in the US Congress for a regulatory pathway, analysts and industry experts are hopeful that such a convergence might boost up the biosimilars space. Above all, an important fact to bear in mind is that all pharma companies have a generic strategy in hand, which will be a big boost for the biosimilar space.

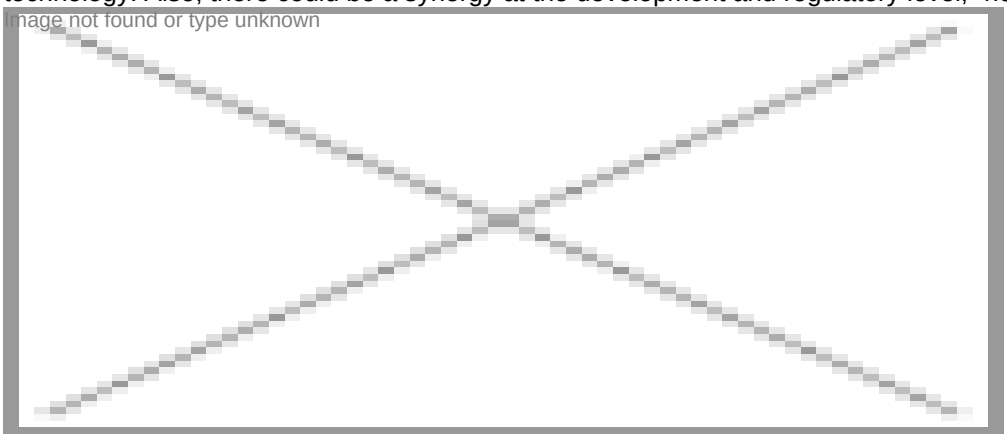
According to Nair, “All the big pharma companies are talking about emerging markets and all of them have a generic strategy now. With generics being the focus for pharma companies, I see a collaboration here which will immensely benefit

biosimilars. That's because biosimilars have much better margins than other generics which will attract big pharma, even while big pharma's commercialization capabilities will give the access and reach to biosimilars."

Integrating the two entities: A major task in hand would be integrating assets of two entities which are in all aspects poles apart from each other. Experts have unanimously opined that companies will prefer to keep assets pertaining to R&D and manufacturing independently.

Ideally, when a pharma company takes over a biotech organization, they try and preserve the culture of the latter, which is more entrepreneur-driven and polished compared to a pharma organization which is more process driven. Integration will ideally be seen in the shared services, human resources and the financial services. The Roche-Genentech integration is an apt example. "Genentech is a fiercely independent company, and even after Roche taking over, its R&D unit has been kept independent," says Krishna.

Singh opines that integration could happen at the sales force and manpower level. "I see integration will mainly happen atthe manpower level and sales force to a certain extent. Manufacturing will be a separate unit because you'll need a different technology. Also, there could be a synergy at the development and regulatory level," he adds.



Company strategies

Pfizer, which has now set its foot in biologics has majorly revamped its business strategies. Following the Wyeth acquisition, it will establish a unique research model designed to advance the strong scientific capabilities of both Pfizer and Wyeth, and to support the new company's nine diverse healthcare businesses. In order to maximize new opportunities in biopharmaceutical research, Pfizer will form two distinct research organizations-—the PharmaTherapeutics Research Group and the BioTherapeutics Research Group. The PharmaTherapeutics Research Group will focus on the discovery of small molecules and related modalities and the BioTherapeutics Research Group will focus on large-molecule research, including vaccines. The new BioTherapeutics Research Group will capitalize on Wyeth's industry-leading expertise in biologics and build on the momentum established by both Pfizer's Biotherapeutics and Bioinnovation Center (BBC), and centers of large-molecule research and pharmaceutical science excellence in PGRD, which will be a part of the new and larger group. This new group's mandate will be to create a broad and deep pipeline in vaccines, antibodies, proteins, peptides, nucleic acids and other novel modalities.

"Creating two distinct but complementary research organizations, led by the top scientist from each company, will provide sharper focus, less bureaucracy and clearer accountability in drug discovery," says Jeff Kindler, CEO, Pfizer, in a press release. The new Pfizer will consist of nine diverse global healthcare businesses. The convergence between the two entities is aimed to capture key therapeutic areas such as cardiovascular, oncology, women's health, CNS and infectious disease; vaccines, biologics and small molecules; and animal health with products for companion animals, consumer health, biologics and anti-infective. Going into emerging markets like China, Latin America and the Middle East is also on the cards.

In order to preserve the 'biotech' work culture of the company rather than diluting it, Genentech's research and early development will operate as an independent center. At present, Genentech's Avastin has been approved in the US and clinical trials are in progress to investigate the efficacy of Avastin in several other tumors. The synergy target increased to one billion Swiss francs annually, and a total one-time integration costs of approximately three billion Swiss francs has been alloted. The combined company has development portfolios with 10 new molecular entities in ongoing or planned late-stage clinical development.

Following the Eli Lilly-ImClone systems deal last year, their combined oncology portfolio will target a broader array of solid tumor types including lung, breast, ovarian, colorectal, head, neck, and pancreas, thus positioning Lilly to pursue treatments of multiple cancers. Partnering with ImClone will expand Eli Lilly's biotechnology capabilities. "We think very highly of ImClone's ground-breaking work in oncology, particularly its success with Erbitux(R), a blockbuster targeted cancer therapy, and its ability to advance promising biotech molecules in its pipeline," says John C Lechleiter, president and CEO, Eli Lilly. This will also help them broaden their portfolio of marketed cancer therapies and boost Lilly's oncology pipeline with upto three promising targeted therapies in phase III in 2009. By bringing together ImClone's and Lilly's oncology products, pipelines and biotech capabilities, the company is taking a step forward in addressing the challenges of patent expirations.

The combined entity of Merck and Schering-Plough will bring in a combined portfolio of products in key therapeutic areas which include cardiovascular, respiratory, oncology, infectious diseases, neuroscience and women's health. Moreover, Merck

will now get a footing in the emerging markets and hence devise a strategy accordingly for these markets because of the fact that Schering-Plough generates more than 70 percent of its revenues outside the US with around $2 billion in revenues coming in from these markets.
The Indian vaccine sector is a growing market and post Shantha-Sanofi deal, analysts predict that there will more such deals in this space to follow suit.

Challenges

Integration of assets of both the entities could be a challenge. Biotech is a different ball game and intellectually they're different from their pharma counterparts. While biotech, which is still in developing stage, is science-driven, pharma is mainly commercialization-driven.
Kar says, "The biotech market is also much more concentrated than the pharma. "The biologics are costly as compared to the pharmaceuticals. We have to really see how pharma companies are moving ahead with the higher prices of biologics to make it a drug of choice, as the convergence will find the pressure both from the government and the consumer to slow down the growth of the healthcare costs," Kar adds.

Looking ahead

With such a convergence, in the near future, one would see fewer pure biotech companies. "Pharma has the money, it has the need to reinvent itself and their solution being biotech and biotech has it own challenges. So, a convergence will be natural. Currently pharma and biotech is fairly distinctive and I see that line getting blurred," adds Nair.
Singh maintains that a major trend would be companies would have a dedicated focus on biogenerics. "Another trend would be that within the fold of a pharma company there would be a separate business units which would focus on chemical as well as biopharma. The marketing strategies might differ because normally biological compounds are driven by value and not volume and there is a different logistics chain which is used for biological compounds," he concludes.
Mixed reactions have emerged within the industry as to whether we can expect to see similar deals this year. There wastalks of Pfizer buying out Biogen but the deal did not take off because of valuations. There were talks of Amgen being acquired as well as Bristol-Myers Squibb. "Small deals will continue to happen. However, I do not expect to see any big biotechs being up for sale. This is primarily because, they have the funds and are public entities," said a research analyst. " There are some big deals bound to happen this year. We can look out for some," opines another analyst from a well-renowned firm.

Nayantara Som