From pharmaceuticals to biotech to healthcare delivery, change is coming fast and furious. Will your organization be ready?

LIFE SCIENCES: Mutating Business Models
In the life sciences industry, we expect market changes to be precipitated by scientific innovation. But over the next decade, the more significant industry developments will likely be driven by business issues: the growth of branded-generic and generic drugs; hostile takeovers in the biotech space; the emergence of the Brazil, Russia, India, and China (BRIC) markets; and shifts in venture capital, R&D spending, and licensing agreements.

Whether you’re big pharma, a biotech startup, a medical device maker, a healthcare provider, or a financial institution that supports such innovation, those changes have implications for product development, organizational structure, go-to-market strategy, and investment planning.

**Come Together: Branded and Generics**

The cost to develop a new drug is $1 billion and climbing. At the same time, major drugs have come off or are coming off patent, and there don’t appear to be many blockbusters in the pipeline. Plus, there has been a clear increase in the number of generic drug companies submitting abbreviated new drug applications (ANDAs) to the U.S. Food and Drug Administration. Those factors are having a significant impact on product development for innovative and generic drug makers alike.
Generics are grabbing market share in countries around the world. The value of the total pharmaceutical market will grow by up to 7 percent in 2011, to $880 billion, according to IMS Health, ahead of a 5 percent pace in 2010. But more of those dollars are going to generics, with $30 billion in developed-market sales threatened by generic competition this year. By 2014, 85 percent of prescriptions could be generics.

Strengthened by their success and looking to spread risk, generics are beginning to compete head-to-head with branded pharma. For example, Israeli generics giant Teva Pharmaceutical Industries is enforcing patents related to drugs such as Copaxone, used to treat multiple sclerosis, and Azilect, used to treat Parkinson’s disease. The company reportedly has several innovative compounds in the pipeline.

But big pharma is fighting back. One way is by entering the generics market themselves. The most obvious examples are Swiss drug maker Novartis, which operates Sandoz as its generics division, and Japan’s Daiichi Sankyo, which in 2008 acquired Indian generic maker Ranbaxy.

There are other tactics for building market share, such as authorized generics. The “first” generic applicant to challenge a listed patent by filing a Paragraph IV certification may be granted 180-day exclusivity before other generics can be launched. But “the branded company can create its own authorized generic to capture market share before, during, and after the 180-day exclusivity period,” explains Cary Miller, Of Counsel for Morrison & Foerster. GlaxoSmithKline, Merck, Pfizer, and Sanofi-Aventis all offer authorized generics.
The branded company can also file a citizen’s petition to try to convince the FDA not to accept or approve an ANDA for a particular drug. In 2003 Sanofi-Aventis submitted a citizen’s petition over Lovenox, a drug for preventing blood clots, urging the FDA to require generics to use a specific chemical profile and follow Sanofi-Aventis’ manufacturing practices. This strategy, in combination with litigation, held off generics till mid-2010, when the FDA OK’d a generic under an ANDA submitted by Sandoz.

Finally, there are direct legal challenges through lawsuits—for example, relating to Paragraph IV certifications. When a generic submits an ANDA, it can file a Paragraph IV certification stating that its drug doesn’t infringe relevant valid patents listed in the “Orange Book” of FDA-approved drugs. The branded company can then respond with a patent-infringement action, which results in a 30-month stay of the ANDA approval—or a launch by a generic “at risk.”

But branded companies need to carefully weigh the costs of a lawsuit against the potential benefits, Miller notes. “Are you going to sue over the first ANDA, and the third, and the 10th?” she asks. “It might be more cost-effective to settle.”

That’s especially true for drugs that target a relatively small base. “There will be increasing litigation over drugs for markets of $50 million or $100 million,” Miller predicts. “Whether you’re a branded or a generic company, you need to determine on a case-by-case basis whether that litigation is worth the cost.”

Generics, for their part, need to watch out for legal challenges. For example, branded companies are changing the formulations or concentrations of drugs in a bid to shift the market to a new “version” of a drug before a generic hits the market. “Look at not only those patents in the Orange Book but also new patents and pending applications by branded companies,” Miller advises. “Monitor patent applications that cover the indications or uses of a drug, as well as changes in formulations coming through the pipeline.”

Biotechs or Bust

Pursuing generics isn’t the only option for companies with expiring patents and empty pipelines. Increasingly, cash-rich pharmaceuticals are on the prowl for bargain biotechnology companies—if “bargain” is the right word, given that the cost of these acquisitions has been rising. (Biotechs are generally defined as companies that develop treatments by manipulating organisms or bioprocesses, as in genetic engineering, though the line between biotechs and traditional pharmaceuticals is blurring.)

For example, in 2009, Swiss pharmaceutical Roche bought out the more than 47 percent it didn’t already own of U.S. biotech behemoth Genentech for $46.8 billion. Then, in June 2010, Astellas Pharma acquired OSI Pharmaceuticals; the $4 billion takeover—the second-largest U.S. acquisition by a Japanese drug maker—was 11 percent higher than Astellas’ first bid three months earlier. At press time, Sanofi-Aventis was in a protracted bid to acquire Genzyme. In April 2009, U.S. biopharmaceutical Gilead Sciences—which itself started out as a biotech—acquired CV Therapeutics in a $1.4 billion deal.

In many of these transactions, the acquirer was after a specific product. “These are really product acquisitions,” says Michael Braun, a partner at Morrison & Foerster who represented Astellas in the OSI deal. “Gilead bought CVT for Ranexa, a cardiovascular drug. Astellas bought OSI to acquire Tarceva, an oncology drug.”

Astellas confirms that this is its general approach to acquisition. “There are really two ways a biotech can make itself an attractive target,” says Naoki Okamura, the Astellas exec who is now head of OSI. “One is to establish a technology platform. But that can be difficult to valuate because it still needs a proof of concept. The other is to develop a promising compound. We typically look for a company that has an attractive compound.”

But Astellas didn’t initiate the deal as a hostile takeover. “It was an unsolicited offer,” according to Okamura. “A hostile takeover should be done only after every other measure is exhausted.”

Why, then, are so many of these tender offers turning into hostile bids? And why now?

“A few things have happened to make tender offers more attractive,” Braun notes. “First, the SEC changed the best-price rule.” In the past, the best-price rule required that the highest price offered to a single shareholder be offered to all shareholders. So if a company offered a target $10 a share and offered the target CEO a consulting agreement job that could be construed to be worth $1 a share, then it had to offer all shareholders $11 a share. Now, such a consulting agreement needn’t be considered as part of the purchase price, “and that makes tender offers less risky and costly,” Braun says.

More specific to the life sciences industry, biotechs have shown themselves to be more innovative than traditional pharmas. And with few or no blockbusters in the pipeline, pharmas have to go outside for innovation.

Finally, a weak global economy means share prices are low compared
to historic levels, and that makes targets vulnerable to tender offers. That’s also why these deals end up being takeovers. Says Braun: “Biotechs have been reluctant to be acquired, because they have a different view of their valuation, based on past prices, than potential buyers.”

Biotechs that want to avoid a takeover can avail themselves of a broad range of legal manipulations, Braun points out. “But ultimately you have to think about stockholder value and do what’s best for stockholders,” he says.

And stockholders tend to drive M&As. When a tender offer is made, shares often trade hands, driving up the share price—the soft economy notwithstanding. And when share price rises, longtime holders cash in. That can leave shares in the hands of arbitrageurs, who typically want to sell quickly.

In any case, the trend is likely to continue. “Major pharmaceuticals have been looking for ways to sustain their own growth, but they haven’t been able to achieve that internally,” Okamura says. “So they have to look for value outside the company, through licensing or product acquisitions or M&As.” As for biotechs, he says, “venture capitalists and institutional investors have most often assumed from the beginning that the destiny of biotechs is to be acquired.”

**Emerging Markets: BRIC or Buoy?**

But far bigger changes loom than those wrought by M&As. The most fundamental shift in life sciences will be the rise of emerging markets, particularly the BRIC countries.

There are 17 “pharmerging markets,” as IMS Health calls them, which are expected to grow by 17 percent this year, to $180 billion. China, which is now the world’s third-largest pharmaceuticals market, will surge 27 percent to exceed $50 billion in 2011 and $100 billion in 2014. Pfizer alone will pull down $3 billion in China by 2012, according to a Goldman Sachs report.

As for medical devices, the BRIC countries represent an $18 billion...
Health Infomatics Boots Up

Information technology was supposed to transform healthcare delivery. But beyond electronic medical records, health infomatics has been more promise than payoff.

That may be changing. New technology, cheap data storage, high-speed connections, and growing demand may be adding up to a perfect storm of IT and healthcare convergence. In fact, the U.S. market for healthcare IT, at $33.9 billion in 2010, will grow 24 percent over the next four years, according to IDC.

The players include small startups and IT-industry behemoths—an indication that many see profits ahead. And their innovative deals and deliverables are just as varied:

- Intel and GE Healthcare are spending $250 million to create and sell home-based health technologies, a deal for which Morrison & Foerster provided both IP and HR representation. The market for telehealth and home health monitoring is expected to grow from $3 billion in 2009 to $7.7 billion by 2012, according to Intel.
- Epocrates offers mobile decision-support tools that help healthcare professionals reduce medical errors and speed care. The company’s solutions are now used by almost half of all U.S. physicians.
- PhysiScore, developed at Stanford University, determines the risk of illness for premature babies. The tool aggregates and evaluates data that’s already being captured, such as birth weight, heart rate, and respiratory rate, to develop a risk profile that’s more accurate than invasive tests.
- AT&T ForHealth, a new division of the largest U.S. telecom, is developing wireless, networked, and “cloud-based” healthcare IT solutions. Examples include medicine bottles that remind patients to take pills, devices that monitor heart levels in the home, and audio-video links that replace doctor visits. AT&T generated $4 billion in revenue from the healthcare industry in 2009.

Many emerging solutions are potential game-changers, especially mobile and telehealth offerings that allow patients to be treated remotely. They also raise questions about who gets paid, and by whom.

Then there are privacy issues. As more patient data is captured, transmitted, and shared, more controls will be needed around what can be used, how it can be used, and who can use it. And there will be disputes over who’s liable in the event of a security breach—the user of the data, the originator of the data, the owner of the network, or the developer of the technology.

“We’re on the cusp of a new era of opportunity,” says Stephen Thau, a partner with Morrison & Foerster. “The winners will be those that fully understand both the IT market and the healthcare market.”

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Big pharma is likely to license up to 70 percent of its pipeline. "That fact will likely divert larger Chinese companies from outbound acquisitions, believes Charles Comey, a partner with Morrison & Foerster who until recently was based in China. "For now, Chinese pharmaceuticals will be focused on domestic consolidation."

And it’s not just pharmaceuticals. The medical-device sector is heating up in China, and Chinese device makers are looking for foreign partners. An example is Mindray Medical, China’s largest medical device company, which has operations in the United States and which recently struck a licensing agreement with Pulsion Medical Systems, a German device maker.

Healthcare delivery is likewise set for tremendous growth. China, for instance, is building 30,000 hospitals, clinics, and care centers across the country, according to Bloomberg Businessweek. "They’re building hospitals and training doctors and nurses," Thurston says. "But they are short on expertise in hospital management." That will mean enormous opportunity for providers of hospital management software and services.

In short, "the growth of the Chinese market is such that every life sciences company needs to have a China strategy," Comey says.

For pharmaceutical companies in particular, entering emerging markets dovetails with the confluence of branded and generics. "Price containment measures in the United States and Europe will drive the generics market," Thurston says. "But you won’t win market share based on low prices in these mature markets."

That means targeting emerging markets, especially with generics.

Entering these countries will likely involve a lot of partnering. "The megamergers of the past couple of years were driven in part by the need to be more globally powerful," Thurston points out. "But following those mergers, companies cut their sales forces." As a result, in some markets they’ll have to work with local distributors as they expand to new markets.

It will also involve legal services. As companies jockey to take advantage of market potential, they’ll be raising capital, filing patents, and entering into research, manufacturing, and distribution agreements.

That will require legal advice from a firm that not only has a specialty in life sciences but also has expertise in emerging markets.

Vested Interests
The changes in the life sciences landscape—colliding innovative and generic drugs, biotech takeovers, emerging markets—are calling for a rethinking of research and development, licensing, and investment strategy. On top of that, there’s increasing demand for first-in-class therapies that address unmet needs, as opposed to me-too drugs that add only marginal value.

But big pharma has been winding down its R&D capability—in part because of price pressures. Government reimbursement programs are exercising enormous downward pressure on prices in the United States, Europe, and elsewhere. As a result, big pharma is partnering with smaller biotechs and universities for research. Going forward, it will in-license more and more of its pipeline—up to 70 percent, by some estimates.

STEM CELL TREATMENTS: Ready for Prime Time?
In the past year, four human trials of embryonic and fetal stem cell therapies began, and others are on the way. That could mean new opportunities—and new legal considerations.

"These developments raise questions around freedom to operate or the ability to commercially produce or market without infringing IP," says Terri Shieh-Newton, a Morrison & Foerster associate. One company might identify its patented stem cell with one set of biological markers and a second company might use another, but "they’re using different markers to identify the same cell."

Then there are regulatory concerns. "It took Geron a long time to get FDA approval to do its trials;" Shieh-Newton points out. "So companies may go outside the U.S. to conduct their first trials." For example, in December, U.S. biotech StemCells Inc. received approval to conduct stem cell research in Switzerland.

But going overseas isn’t easy. "Each country has its own regulatory requirements," notes Paul Claydon, a Morrison & Foerster partner. "Because these therapies are so novel, there are often additional approvals required."

In the U.K., for instance, in addition to Clinical Trials Regulations, stem cell research must be approved by the Gene Therapy Advisory Committee.

Research is moving forward, and new developments will mean new opportunities. "Stem cells will be tested in areas that have been unresponsive to conventional treatments," says Michael Hunt, CEO of ReNeuron Group. In November, his company launched the U.K.’s first trials using fetal stem cells to treat stroke patients. "This will have a significant effect on life sciences," he says.
“Big pharma is looking for opportunities to combine their own assets with in-licensing or acquiring product rights from third parties,” says James Ryan, an associate at Morrison & Foerster. “But more than that, they’re changing the way they deal with these third parties. Five years ago they might have gotten involved after Phase II trials. Now they’re looking to take control of the development program much earlier.”

A few examples of these new collaborations:

Pfizer Regenerative Medicine is joining with University College London to pursue stem cell therapies.

Pfizer is also working with the University of California, San Francisco, to target the “Valley of Death” stage of development between early scientific research and marketable treatments. Pfizer will pay up to $85 million over the next five years if the partnership leads to significant new therapies.

Denmark pharma Lundbeck and King’s College London have launched a research collaborative that will involve AstraZeneca, Eli Lilly, GlaxoSmithKline, Novartis, Pfizer, Roche, and others. The program is being funded with $33 million from the EU’s Innovative Medicines Initiative.

Sanofi-Aventis is expected to pay up to $2.2 billion to contract with research organization Covance in a 10-year R&D outsourcing deal.

Universities, for their part, are increasingly funding their own innovations and then licensing directly to big pharma, rather than relying on venture capital. Meanwhile, large charities are getting directly involved in R&D. An example is London-based Wellcome Trust, which has pumped $30 million in Series A equity funding into Kymab, a biopharmaceutical.

What’s more, big pharmas are cooperating. In late 2009, archrivals Pfizer and GlaxoSmithKline launched ViiV Healthcare, a joint venture focused on HIV treatments. “There’s a blurring of the lines in who deals with whom and who funds whom between and among big pharma, biotechs, and universities,” Ryan says. “That’s true in terms of who does what, such as discovery or clinical work or licensing. And it’s true in terms of who targets which markets.” For example, a biotech might get upfront funding from a big pharma, retaining rights in emerging markets while ceding rights in the United States or Europe.

Finally, pricing pressures are driving companies to invest in “orphan drugs” that target rare conditions. “The shift toward reimbursing only superior outcomes means me-too drugs aren’t going to be profitable,” explains James Gubbins, a partner at Morrison & Foerster. “Even though there’s a smaller market for orphan drugs, the reimbursements are much higher.” It’s no surprise that the global market for orphan drugs has been growing at a compound annual rate of about 7 percent for several years and is expected to reach $81.8 billion this year, according to BCC Research.

The life sciences industry is increasingly mature; the biotech segment is now 30 years old. It has reached the point where change will be driven as much by business issues and economic factors as by scientific innovation. Over the next decade, the organizations that best adapt to mutating business models will be the ones that achieve new levels of success.

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