The keys to successful entry into the US market

How can crowdsourcing help drug development?

Make the most of your forgotten assets
While many pharmaceutical company executives blame their woes on increased regulatory scrutiny, escalating labour costs, downward drug pricing pressures and generic drugs, a new analysis suggests the current troubles can be primarily traced to flawed and outdated business practices.

**Lack of innovation and productivity**

A recent analysis by Bernard Munos, founder of InnoThink, a partnership to advance drug research into breakthrough innovation, finds that, from 1950 to 2008, the US Food and Drug Administration made 1,222 approvals of new drugs (1,103) and biologics (119).

Interestingly, over the same period, the annual investment into new drug research and development dramatically increased, growing at an average compounded rate of 12.3% per year, according to the Pharmaceutical Research and Manufacturers of America (PhRMA), reaching roughly $50 billion per year today. Despite this massive R&D investment, the number of new drugs approved each year over the past 50 years or so has remained fairly constant, averaging around 25 to 30 per year. In other words, spending more on R&D initiatives has not improved innovation or drug development productivity in the life sciences industry.

In addition to stagnant productivity and a lack of innovation, today’s pharmaceutical industry faces several other challenges. Longer R&D cycles and increasing regulatory scrutiny are causing R&D costs to spiral out of control. Also, the impending patent expiry of many blockbuster drugs (those exceeding annual revenues of $1.5 billion) threatens to cut total drug sales revenues by as much as 41% by 2015. Indeed, by the end of 2012, 20% of big pharma’s current sale revenues will be susceptible to generic drug encroachment. Generic prescription drugs are expected to represent 17% of total global pharmaceutical sales by 2014, up from 10% in 2008. Finally, healthcare reform legislation and increasing downward pricing pressures imposed by insurance companies and third-party payers are driving down drug reimbursement costs and squeezing the profit margins of many branded prescription drugs.

Drug makers have attempted to adjust by controlling costs through job cuts, corporate restructuring and M&As. For example, over the past four years alone, the world’s ten largest pharmaceutical companies have eliminated more than 200,000 jobs – 18% of the 2010 aggregate global pharmaceutical workforce.

During the same period, M&A activity has skyrocketed, with several major acquisitions taking place, including Pfizer/Wyeth and Merck/Schering Plough, as big pharma companies scurry to bolster their biotechnology product offerings. While both strategies are likely to help to control costs and boost company stock prices in the short term, neither is likely to help to improve productivity nor spark the type of innovation that is drastically needed at most big pharmaceutical companies.

**About the author**

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End of the blockbuster model

There is a growing consensus among pharmaceutical company executives and industry insiders that the blockbuster drug business model is no longer viable in today’s highly competitive global marketplace.

According to a study of recently approved drug sales (329 for which data were available) conducted by InnoThink, the probability that a new molecular entity (NME) will achieve blockbuster status is approximately 21%, a success rate that has not changed for the past 20 years, even with massive financial investment into pharmaceutical R&D.

Despite this historically low success rate, most big pharma company executives have nevertheless continued to rely on the blockbuster drug model as the main business driver. In fact, a plethora of anecdotal evidence suggests the blockbuster mentality either hindered or killed the development of many innovative and potentially beneficial NMEs simply because they lacked true blockbuster potential.

There is general agreement among most industry analysts that big pharma companies must move with the times to remain productive and relevant. Recommended changes include:

• improved R&D productivity
• continuation of drastic cost-cutting
• formulation of a strategy rapidly to garner market share in emerging markets

While some analysts contend that conventional M&A strategies can address these issues, there is a growing consensus that fundamental changes to big pharma’s business model are going to be necessary to ensure its survival.

Among those who have been calling for seminal changes for some time is Jean-Pierre Garnier, the former CEO of GlaxoSmithKline (GSK). “The leaders of major corporations, including pharmaceuticals, have incorrectly assumed that R&D was scalable, could be industrialised, and could be driven by metrics and automation,” he said in 2008. “The grand result: a loss of personal accountability, transparency, and the passion of scientists in discovery and development.”

More recently, John Lechleiter, CEO of Eli Lilly, echoed similar sentiments when he declared that: “At a time when the world desperately needs more new medicines, we’re taking too long, spending too much, and producing far too little. The engine of biopharmaceutical innovation is broken.”

InnoThink’s Munos predicts the lack of innovation in pharmaceutical R&D will probably cause “an implosion of the old model” of drug discovery and development within the next three years.

Open innovation

Historically, the life sciences industry has operated by using a ‘closed innovation’ business model, where ideas are generated internally and ultimately commercialised using vertically integrated internal corporate resources. This process is mainly driven and protected by patents and intellectual property.
At a time when the world desperately needs more new medicines, we’re taking too long, spending too much, and producing far too little. The engine of biopharmaceutical innovation is broken.
a proprietary software platform that allows participants selectively to share collaborative drug discovery data. Other big pharma companies, including Pfizer, Merck, and Johnson & Johnson, have also shown a willingness to participate in various open innovation projects like the Sage Bionetworks, the Neglected Tropical Disease Global Network, and the International AIDS Vaccine Initiative.

Crowdsourcing drug development

Most of big pharma’s experiments with open innovation have almost exclusively focused on drug discovery, the first step in the drug development process, probably because this is the least regulated part of the pharmaceutical drug commercialisation process. But, while significant financial investment is needed for discovery research and preclinical drug development, the most costly part of the commercialisation process is usually human clinical trials. These costs are rising, mainly because of regulatory agencies’ increased emphasis on drug safety.

Some analysts contend that clinical development represents as much as 33% of today’s total drug R&D costs. InnoThink’s Munos determined that, to garner regulatory approval for various indications for three blockbuster cancer drugs, Avastin, Erbitux, and Rituxan, approximately 387, 125, and 100 clinical trials, respectively, were conducted. The UK-based research firm CMSInfo calculated that spending in 2005 on US clinical trials was nearly US$24 billion. This amount is expected to exceed US$32 billion by the end of 2011.

Tomasz Sablinski, Managing Director at Celtic Therapeutics (a private equity drug development firm) and chief architect and founder of Transparency Life Sciences (TLS), suggests that applying a crowdsourcing and open innovation model to human clinical trial design could cut costs and increase efficiency in the clinical drug development process.

Sablinski, a former clinician with more than 12 years of experience managing clinical drug development at several major pharma companies, contends clinical drug development costs are skyrocketing and efficiency is falling because pharma has been forced by mounting financial pressures to outsource many clinical trial activities to chief research officers (CROs).

“While CROs are happy with their current workloads, the growing number of new drugs entering clinical development has resulted in longer clinical development times and more costly trials,” says Sablinski. “There is an enormous amount of untapped clinical development and trial design expertise out there. Why not take advantage of it?”

The TLS open innovation model aims to combine the collective knowledge of a network of veteran clinical drug development individuals and firms with the latest advances in biosensors, wireless home-health devices, medical software apps and telemedicine (distance medicine) technologies. Sablinski believes he can use this approach to speed clinical development and identify new uses for or repurpose discarded NMEs or previously approved prescription medicines. The centrepiece of TLS’ unique approach is a robust, collaborative intelligence, web-based system. This system, which is under development, will help TLS to manage electronically the interactions between the company and external contributors, and capture, analyse and refine the collective knowledge of the TLS community.
Due to the nature of pharma, an ‘open source’ or ‘pure virtual’ open innovation model seems unlikely to be a viable option.

“The obvious place to start is finding new clinical indications and uses for generic drugs,” says Sablinski. “We already know a lot about their modes of actions and safety profiles, and repurposing them for other indications has a higher probability of success than developing new or novel drugs.”

Sablinski’s “drug repurposing” idea is not unprecedented. According to Munos, researchers at the Institute for Advancing Medical Innovation at the University of Kansas “are working on several molecules, including one that is an old antifungal that has been found to be highly effective against some types of cancer”.

Support for Sablinski’s concept has been growing since he introduced it several years ago at a number of open innovation conferences. Munos thinks the idea is a “potential game changer”.

Daniel Reda, entrepreneur, IT expert and Co-founder of CureTogether.com, a patient-focused drug development website, says: “Tomasz’s approach, if it works, would give previously discarded or undeveloped expensive drugs a chance to positively impact many lives.” Others applaud Sablinski’s attempt to improve clinical drug development by integrating cutting-edge mobile healthcare and monitoring technologies into the clinical drug development paradigm.

Some, though, remain unconvinced. Jean-Jacques Garaud, Head of Roche Pharma Research and Early Development, contends the crowdsourcing concept is not new and is already part of established pharma R&D activities. “Companies already source ideas, technologies, compounds et cetera from an external network of contributors that includes academic groups, service providers, and biotechnology companies,” says Garaud. “The difference between this and Sablinski’s approach is the use of new technologies and tools that expand the network’s reach, improve flexibility and simplify reward mechanisms for contributors.”

“Due to the nature of pharma – for example high costs, high risk, regulatory constraints – an ‘open source’ or a ‘pure virtual’ open innovation model seems unlikely to be a viable option,” Garaud warns.

Crowded out?

Open innovation drug discovery models are unquestionably gaining traction at several major pharmaceutical companies. However, major challenges stand in the way of their wholesale adoption by the industry.

Firstly, open innovation is likely to elevate the regulatory requirements associated with drug development because of the number and increased diversity of contributors to the process. Consequently, implementation of the model would require careful design, ongoing and regular contact with regulators, and a large investment and commitment of overhead in project management and information technology support.

There are also concerns about how patents and other intellectual property generated during the open innovation process would be handled and managed; who will own the patents? While patents and IP are the lifeblood of the life sciences industry, Jackie Hunter, Senior Vice President of Science Environment Development at GSK, contends...
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that wholly owned IP does not always automatically lead to success and creation of commercial value. For example, she noted in a recent publication that large companies typically commercialise a miniscule portion of their patent portfolio. Contrary to popular belief, Hunter claims, open innovation can actually drive IP creation. But for this to work correctly, she stresses, all contributors must agree at the outset of the project on patent ownership, and all commercialisation and royalty-sharing provisions.

Complex payment system
In addition, open innovation is likely to require an unusually complex reward system for contributors, including fees for service, fees for success, and milestone and royalty payments. Which open innovation contributors will provide the initial capital investment to drive projects, and how will monies be disbursed to individual contributors if a project is successful? Some open innovation advocates contend that the use of in-kind contributions, such as access to tools, reagents and expertise, can obviate the need for up-front cash contributions and help to manage the reward system. Whether this idea is viable remains to be seen.

Open innovation proponents contend that the process is designed to help mitigate risk by distributing it among individual network contributors. However, the increasing risk-aversion of big pharma companies represents to many the greatest impediment to adopting the open innovation model for pharmaceutical drug development and commercialisation.

It is too early to know if open innovation will become an integral part of new drug development, but Roche's Garaud believes it has the potential for growth in a variety of areas, including:

- exploratory research and entry into new therapeutic areas
- support for niche or developing technologies
- sourcing solutions for chemical synthesis, assay and animal model development, and biomarker identification/validation
- repurposing of molecules for new indications and combination drug therapies
- innovative marketing
- drug safety and postmarketing surveillance.

Open innovation in the pharmaceutical drug development process may have an uncertain future but big pharma’s business model is in desperate need of repair. Without rapid action, pharmaceutical companies may soon be unable to discover and develop the innovative, new medicines that are required to address unmet medical needs.