Using Open Innovation to Tackle the Dearth of Antibiotics

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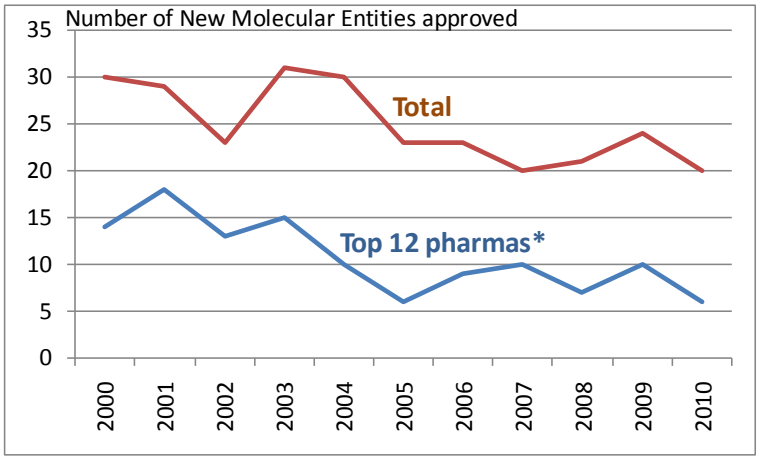
This paper was prepared to accompany a presentation made at the ReAct conference on "Collaboration for Innovation - The Urgent Need for New Antibiotics" in Brussels, on May 23, 2011

Abstract

Despite bulging new drug pipelines, the pharmaceutical industry faces the most severe innovation crisis in its history. This has resulted in a dearth of novel antibiotics, and a retrenchment of pharma R&D from several other therapeutic areas. The facts suggest that, contrary to what is commonly thought, this crisis is not attributable to a shortage of funding or to overly cautious regulators. Instead, the industry R&D model, which for the last 15 years has strived to minimize risk through the disciplined application of strict processes, has become increasingly unable to deliver breakthroughs. This paper reviews the facts and suggests that harnessing the strengths of open innovation could be an effective and economical way to revive anti-infective innovation.

The pharmaceutical industry is in the midst of a severe innovation crisis. The number of new drugs licensed to large companies, fell to an all-time low in 2010 (fig 1), and is no longer enough to replace sales lost to generics. In the United States, 22 of the top 25 most prescribed drugs are now generic, and 78% of prescriptions are filled by generics, a figure that is expected to rise to 90% by 2013.

Figure 1: New Drugs Approved by FDA: 2000-2010



*Includes their cohort of acquired companies

Source: FDA

This failure to innovate is often blamed on regulators or complex science. The data, however, suggest another explanation, that of a business model that is failing before our eyes. It failed first with antibiotics ten years ago, when the industry largely walked away from developing new anti-infectives. And It failed again more recently

when it deprioritized drugs for mental illnesses[1], and cardiovascular diseases[2]. Under pressure to improve performance, drug companies have become more cautious, and redirected their R&D spending towards "safer" programs, those involving known drug classes and targets, that are thought to be less likely to fail. Unfortunately, they are also less likely to produce breakthroughs, often delivering instead tepid incremental innovation, which finds it increasingly hard to gain acceptance from regulators and payers, or to compete in an largely commoditized marketplace.

Big pharma's risk-aversion has narrowed the scope of translational research, leaving on the shelf cutting-edge discoveries, such as nanotechnology, synthetic biology or stem cells, that are thought to be too speculative to warrant significant research investment. It has also kept many companies from engaging in novel R&D models, such as collaborative open innovation models, despite their potential for exploring new hypotheses, eliminating costly duplication, or conducting research in new and more efficient ways.

The result is an industry that treats fewer patients with increasingly unaffordable drugs, and shuns the novel innovation pathways and ideas that it needs to deliver more breakthroughs. Risk-avoidance has paradoxically resulted in greater risk exposure.

This is unfortunate as the industry's achievements over the last century have clearly demonstrated that breakthroughs result from engaging in high-risk, unconventional research[3]. To escape marginalization, and reclaim its role as one of the great contributors to human welfare, the pharmaceutical industry must change its course, and re-engage in high-risk translational research on a large scale. It must do so by joining hands with numerous partners to create broad portfolios of potential breakthroughs, and pay for this shift of resources to early discovery by embracing efficient open innovation models, restricting clinical research to genuine breakthroughs and de-funding other projects.

Open innovation is a catch-all term that designates R&D models that share key characteristics, such as an internet-based network architecture that connects partners located around the world, who collaborate on addressing problems in which they share an interest. These collaborations can involve financial compensation, or simply rely on volunteer contributions from participants. Examples include:

- The Open-Source Drug Discovery initiative (OSDD.net). It is a computerized platform, that allows over 3,500 scientists around the world to collaborate in the discovery of new antibiotics for tuberculosis. It breaks down the drug discovery process in 10 "work packets" such as target identification, assay development, etc. Each "packet" is organized around a wiki. Volunteers choose the packet that matches their expertise, and are thrust in conversations to which they can add their own insights. The platform was launched in 2008 by India's Council for Scientific and Industrial

[1] Insel T., Who Will Develop the Next Generation of Medications for Mental Illness? (2010), available from the National Institute of Mental Health Website [online] <http://www.nimh.nih.gov/about/director/2010/who-will-develop-the-next-generation-of-medications-for-mental-illness.shtml>

[2] Garber A.M., An Uncertain Future for Cardiovascular Drug Development. N Engl J Med. 360, 1169-1171 (2009)

[3] Hollingsworth, J.R. A path-dependent perspective on institutional and organizational factors shaping major scientific discoveries. In Innovation, Science, and Institutional Change (eds. Hage, J. & Meeus, M.T.H.) 423–442 (Oxford University Press, Oxford, UK, 2006)

Research. It runs with 5 full-time employees and an annual budget of $2m. In 2010, 830 volunteers joined hands to re-annotate 85% of the genome of Mycobacterium tuberculosis in 4 months (an effort equivalent to 300 man-years of effort). It has identified 18 novel targets and several drug leads, which are being tested by clinical research organizations in its network.

- Public-Private Partnerships are "bare-bone" organizations of a few dozen people. They were created 10 years ago at the behest of WHO to revive drug R&D for neglected diseases (TB, malaria, leishmaniasis, etc). They typically solicit novel research ideas over the internet, and a Scientific Advisory Board decides what gets funded. Projects are then pursued through a network of partners. For instance the Medicines for Malaria Venture has about 50 employees who run dozens of trials through a network of 130 partners in 43 countries. Its annual budget is about $55m, 87% of which funds research. Its cumulative spending over the last 10 years is $311m, to which one must add an equal in-kind contribution from several big pharma partners such as GSK and Novartis. It has brought Coartem to the market, and is investigating a portfolio of 52 projects, ranging from discovery through registration, and spanning 19 new classes of drugs.
- PD^2 (for Phenotypic Drug Discovery) was launched by Eli Lilly and Company on 2009. It invites the chemists of the world to submit compounds that Lilly assesses for activity against several diseases for which it has developed screening assays. The testing is free with no string attached, and any IP remains the property of the chemist who submits the compound. The hope is that if efficacy is detected, Lilly and the chemist will negotiate an agreement, but there is no obligation to do so. During the first 18 months, hundreds of chemists from dozens of countries submitted over 32,000 compounds. 93 were selected for an in-depth assessment, and Lilly licensed 3 of them, with 3 more under negotiation.
- Innocentive is an electronic exchange that connects companies facing scientific challenges with a worldwide community of over 250,000 "solvers". Firms post their challenges, along with what they are willing to pay for a solution. An email go to the solvers, who decide whether to engage. Proposed solutions are reviewed by the "sponsor" who selects the winner, if any. The IP is transferred to the firm when the award is paid. The data show that about 50% of challenges are solved. No money is paid unless a solution is found. Over the last 10 years, nearly 900 challenges have been solved for about $7m in prizes, representing cost-savings of over 95% to the sponsors. Innocentive has about three dozen employees.
- DARPA is the innovation engine of the US military. Over its 52-year existence, it has brought to the world a series of stunning innovations that have changed the way we work, shop, communicate, create, and entertain ourselves. Its most celebrated contributions include the internet, the GPS, night vision, supercomputing, and biosensors. Yet, DARPA is only 140 "mad scientists", who work with no facilities of their own (beside an office building) on a budget smaller than the R&D spending of a mid-size pharmaceutical company. It has succeeded by espousing a series of unique management principles. For instance, by law, DARPA can only fund disruptive ideas. In the life sciences, these include prosthetic limbs that are controlled by the brain, or treatments to re-grow limbs lost to injury. 98% of its spending funds research.

These examples establish several principles that are important to addressing the dearth of new antibiotics:

1. Innovation *does not scale* with money or people. Just the opposite: money numbs it, and people dull it. Some of the most innovative organizations in the world are very small, and run on shoestring budgets.
2. Marginal innovation is expensive, breakthrough innovation is much cheaper. The corollary is that funding should be restricted to breakthrough ideas and projects, that is those which represents such therapeutic leaps that they rally physicians, patients, and regulators.
3. Breakthrough research cannot be scripted by a code of "best practices". It involves unique challenges that do not lend themselves to process optimization. Funders should be wary of supporting innovation models where research is regimented.
4. Networks are an essential driver of innovation. They excel at uncovering and nurturing novel ideas. They also operate very efficiently.
5. Finally, risk is an essential part of innovation, and should not be avoided. Instead, it should be embraced, and mitigated. Given the probabilities that underpin drug R&D, the only way to achieve effective mitigation is to assemble broad portfolios of potential breakthroughs, that dwarf what single companies have historically been able to generate internally.