



A new framework for radical change in pharma's R&D organization and decision making—and a practical approach for achieving the transformation

Changing pharma's innovation DNA

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It's no secret that Big Pharma's traditional research and development (R&D) engine needs a complete overhaul. What's surprising is how long the industry's taking to fix the problem. Despite a number of bold efforts to bring pharma R&D back to higher productivity levels, the pace of innovation remains anemic: the long-term average lags at one new molecular entity (NME) a year per company. Despite R&D spending at a high 18 percent of revenues, Big Pharma's R&D productivity declined by 20 percent between 2001 and 2007¹. The cost of bringing a new drug to market currently runs at more than \$2 billion, clearly an unsustainable level. Mergers and acquisitions and the creation of mega-companies have not compensated for the slowdown in innovation. As a result, analysts lowered expectations and now hope the global pharma industry will at least eke out a compounded annual growth rate of 1 percent in revenues over the next five years.

Faced with patent expirations, rising expenses, competition from generics and pressure on branded drug prices, Big Pharma's revenue gap could balloon to almost \$100 billion by 2014. For the top 20 biopharma companies in the world, this represents an annual earnings decline of 8 percent. Most companies find that even shopping for innovation externally cannot help close the gap. Recent Bain analysis of 6,000 biotech projects, available for late-stage licensing, shows that only about 200 are likely candidates for a large pharma company. Of these, fewer than 100 show poten-

tial to become top-sellers and taken together, they account for only about \$30 billion in potential revenue.

Pharma companies are striving hard to stave off the R&D crisis through mergers and acquisitions, geographic expansion, and diversification into new areas like consumer health. But they recognize that while these efforts yield more predictable sales in the future, they have limited impact on the profit gap. The US, Japan and Western Europe still account for 80 percent of the global market and recent growth in emerging markets cannot replace lost revenues or profits. Diversification into other healthcare businesses does not help fill the profit gap either, as over-the-counter medications have much lower margins compared with prescription drugs.

With the innovation burden hanging heavy over the industry, many companies have started to experiment with new R&D models. GlaxoSmithKline (GSK) restructured its R&D centers to emulate biotech R&D principles. Still a work-in-progress, GSK hopes to replicate an entrepreneurial culture in a large pharma organization. Eli Lilly acquired ImClone to source innovation from outside the company and then left it as a stand-alone unit operating independently. Pfizer and GSK broke down corporate barriers to share intellectual property and assets to develop new drugs for diseases like HIV. Several pharma companies are partnering with leading academic institutions to promote innovation from basic research. However, the jury is still out on whether these efforts prime the innovation pump enough.

Instead, our analysis as well as a survey by Bain & Company of 20 leading global innovators—responsible for some of the greatest breakthrough medicines in the last few decades—suggests that Big Pharma needs to do even more. The efforts made so far point the industry in the right direction; now companies must press ahead to go much further. They need to

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break through the barriers that currently hold them back. To raise innovation returns back to the level in the era of blockbusters, pharma companies need *transformational* change: change that renews R&D but also cuts across the entire company. Such radical change goes to the root of the problem and explores what holds back innovation—and identifies what can be done to create a vibrant new culture of innovation across the organization. It requires hard decisions to give up entrenched legacy behavior, but also it requires an openness to bring back what worked in the past.

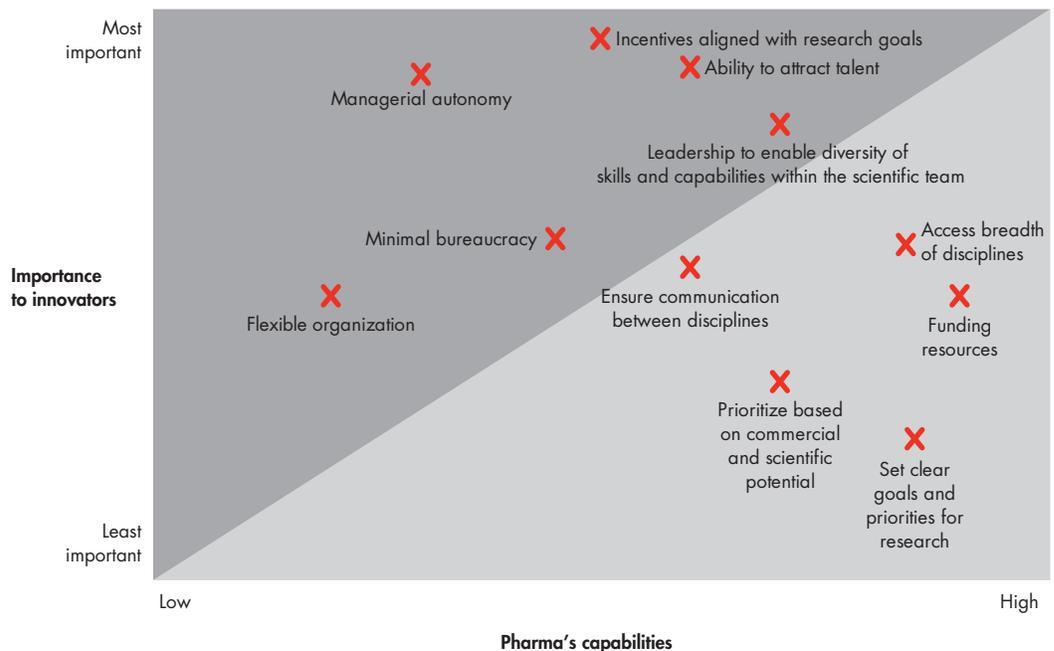
By nature, such change is difficult and takes time to implement. Inevitably, it pre-supposes strong leaders who persevere. In the following pages, we share the findings of our research, develop a new framework for radical change in pharma’s R&D organization and decision making—and offer an approach on how to achieve the transformation.

The innovators’ perspective

To understand what ails pharma we spoke to innovation leaders with a proven track record of creating breakthrough medicines. They brought to the discussions a deep knowledge of academia, venture capital and the current state of biopharma discovery and development capabilities. We conducted in-depth interviews to probe for what they considered key success factors for innovation. We then asked them to rate each factor on its importance. Finally, we asked them to identify the strengths and weaknesses of biopharma companies compared with these factors (see Figure 1).

First, the good news: These innovators strongly believe in the potential for future innovation. They see no set limit to how many new products biopharma companies can develop per year. Nor do they believe the industry has run out of technological advances required to develop new products. They identify two critical areas

Figure 1: Feedback from innovators: Pharma’s current strengths lie in areas that matter less, comparatively, for innovation



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for the success of new product development, in which pharma excels: raising funds and providing access to technologies. They also credit Big Pharma with superior skills in strategy and pipeline management—but herein lies the rub: They rank these two skills as least important for success in innovation.

According to the innovators, the other pressing areas of improvement for pharma companies, in order of importance, are: increasing managerial autonomy; aligning research goals with incentives; attracting and retaining the right, creative talent; minimizing bureaucracy; and creating flexible organizations. In addition, when pressed to identify why in recent times pharma companies struggled to innovate successfully, the innovators identified some common themes.

- Scale crept into every aspect of the business. In the 1980s, when Big Pharma produced blockbusters with much greater frequency, internal champions often led innovation. These leaders could rally the troops across functions and shift the focus of R&D efforts nimbly. Then began the industry's quest for repeatability and efficiency—an industrial manufacturing approach focused on “throughput” and “risk mitigation.” Repeatable processes delivered a host of benefits for Big Pharma. For example, the industry found a steady source of revenue in marginally-differentiating products and making them “evergreen” through extended releases or co-formulations. But innovation suffered when eventually, pharma companies tried to industrialize even the non-scalable, truly creative steps in product generation.
- The vision of success in drug discovery and development got diffused by averages and probabilities. Investment decisions in pharma companies shifted to a “numbers game.” As ideas for drug innovation funneled through several stages, pharma companies measured success in terms of progression from one gate to the next. At the level of the organization, increasingly,

incentives got aligned with annual throughput. Subtly, that shifted the pressure on numerical outcomes: Getting the project to the next phase became as important as getting it right.

- As they grew more complex, pharma companies became risk-averse. As the stakes rose, at every gate, research projects got more input and feedback from various functions across the pharma company: The marketing department weighed in, the strategy team pitched in with a portfolio-management lens, and cross-functional committees became routine. Over time, this created a bias to minimize risk. Truly game-changing projects, with a perceived lower probability of success, struggled to survive the funnel. The more the system rewarded the same way of doing things, the more the odds stacked against rule-breakers. In a world of scientific breakthroughs, however, pharma companies needed more discontinuities and disruptive ideas for successful innovation.
- Many pharma companies grew too big to be effectively managed as one organizational unit for innovation. Today, pharma pursues scale on several dimensions: a global footprint, a diversified product portfolio, influencing new stakeholders and dealing with stricter regulatory requirements. Most of this requires building additional internal capabilities—and a large part of pharma's rising expenses now go to supporting scale, rather than innovation.

For most innovators, a “broken innovation culture” lies at the core of pharma's problems. The rest they cited as symptoms: the lack of dedication to deeply understand the disease biology; the inability to engage in “true” partnerships with academia and biotech; the substantial turnover at the R&D executive level; and a lack of passion to explore new ways to undertake R&D. A majority of the innovators believe that to stoke innovation, biopharma

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must rethink how to reward the right behaviors and create the required flexibility within the organization structure. Says a biopharma head of research, with two successful biotech ventures to his credit: "It all goes back to incentives. If you do that well, you wipe away the red tape." Another successful biotech entrepreneur adds: "Leaders in R&D should have the autonomy to make decisions on how to use funds and allocate resources between programs. They should be able to hire the right number of right people, and not have to staff research projects with whoever is available."

New approach to innovation

It goes without saying—but it also bears repeating—that only leaders can bring about transformational change. Over the next few years, Big Pharma leadership will face two tests: First, reigniting innovation such that it leads to the creation of new, discontinuous technologies. Second, morphing the current organization structures into new forms that nurture discovery and development—and result in new business models. Speed will be important as most leaders will not have the luxury of coming into an organization and learning how things are done. Successful leaders will need to recognize the right moment and grasp it to launch such radical change. In the case of one mid-sized European pharma company for example, the timing coincided with its acquisition of another European pharma company.

The acquiring company used the integration process as a proxy to fully redesign its R&D approach. It set itself a new goal: to achieve an optimal balance between portfolio assets and fixed operating costs. Its new R&D approach was not just highly selective—the company now only pursues opportunities with real medical differentiation—it was also purely priority-driven, so that only valuable projects got resources. To achieve these goals, the acquiring pharma company took nothing for granted while creating a lean, scalable and flexible organization. It retained in-house critical core capabilities

in select areas of discovery, development and life-cycle management. In other areas it partnered with contract research organizations. Today, the combined company's fixed assets account for less than 50 percent of its total resource needs—which, compared with competitors, leaves much more available for research.

Of course, no one innovation model will fit all pharma companies. However, we believe in the future, successful pharma innovators will share three common fundamental principles.

1. They will pursue medical differentiation

As a generic standard-of-care settles in for many diseases, pharma companies will need a higher degree of medical differentiation to successfully introduce new products into the market. This isn't a new idea. In the 1990s, the pipeline for cancer treatments got crowded with pharma companies developing new chemotherapies, most with little therapeutic difference. However, instead of becoming a "me too," Genentech concentrated on changing the way cancer is treated. With the help of PDL's humanization technology, it developed treatments based on humanized monoclonal antibodies—a technology that most pharma companies considered too complicated. The company's researchers focused on understanding tumor biology and set goals to take patient outcomes to a new level. Genentech's reward: Its innovative approach helped it gain market leadership. In addition, Genentech was able to price its therapies several times higher than pharma's marginally improved options.

In today's market, differentiation is more important than ever. Now, increasingly, Big Pharma's customers are payers (very often government customers) and patients who care about two criteria: health outcomes and affordability. Further, it's a much more transparent marketplace. Government agencies develop cost-effectiveness studies; private payers invest in health technology assessments and analyzing real-life medical data; and most information

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is available on the Internet. This new reality has a number of implications for innovation in biopharma companies. First, servicing the new customer requires an innovation engine that produces cost-effective, tangible improvements in healthcare. That, in turn, requires a whole new decision-making process, especially in the early stages of R&D. For example, to ensure that a drug is priced right at the time of its launch, a pharma company might explicitly include early-stage hurdles to test for cost-effectiveness.

Second, pharma companies will need to review portfolios to identify opportunities where they are better off collaborating versus investing in differentiation. Already, the market is less willing to pay pharma companies to develop similar, marginally different products that require a huge amount of competitive marketing spending for promotion. Some pharma companies have taken steps to pool resources—more such collaborative models will evolve in the future. And third, pharma companies will need new criteria and processes for evaluating their pipeline. As companies consciously shift a significant portion of their R&D budget to potential game-changers, by definition, they will take on more risk. To buffer against risk, companies will need to adapt their current approach of treating all projects in the pipeline as equals. Instead, they will move closer to the way investors manage a portfolio: balancing low-risk, low-return assets with high-risk, high-return assets.

2. They will invest in building flexible organizations

Leading pharma companies will be the first to admit that often, decisions suffer death by committee. The malaise is not uncommon: As organizations grow and expand, they adopt more complex structures and processes. Over time, complexity becomes a drag on the quality and speed of decision making. Ineffective decision making can stifle innovation. Pharma companies need to test early and consistently

for what really matters in a drug-development project. For this, they need to have incentives in place to get to the right answer and set the right research goals. While killing a project early—especially for mediocrity—is hard for most organizations, in pharma it's critical for continuous, successful innovation.

In our survey, industry experts stressed that Big Pharma must develop incentives that reward rapid learning, testing and adaptation from pilot projects. But that requires delegation in decision making, which is hard to do if a pharma company is dependent on centralized processes. To get around the issue, a pharma company can view all projects through an investment lens: allocate resources based on pre-determined proof-points; delegate authority down the line to people running the innovation processes; and increase autonomy in areas like outsourcing or staffing decisions.

To make the approach work, a good first step will be to dismantle the pharma company's functional staffing model and replace it with a more flexible human resource model. Under such a structure, empowered project champions can freely use their budget to find the right skills and resources, which might come from within the organization or outside. Some companies like UK's Vernalis or Big Pharma-backed initiatives like Chorus have established virtual development as a viable and often more effective and efficient development model.

Such companies don't just manage costs better by limiting full-time employees, reducing fixed assets and clamping down on overheads; their flexibility and lean structure helps them hone in on successful innovation or quickly move on to the next promising idea. Chorus, which was set up by Eli Lilly as an autonomous division, advanced more than two dozen molecules through candidate identification and Phase I, at median cycle times that were 40 percent to 60 percent faster than the industry average. According to one innovator we surveyed, outsourcing became a learning tool for the organ-

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ization. Says he: “Large, readily available internal resource pools dull the mind and drive the decision to action rather than thought. With outsourcing, the process is reversed.”

3. They will balance the use of scale

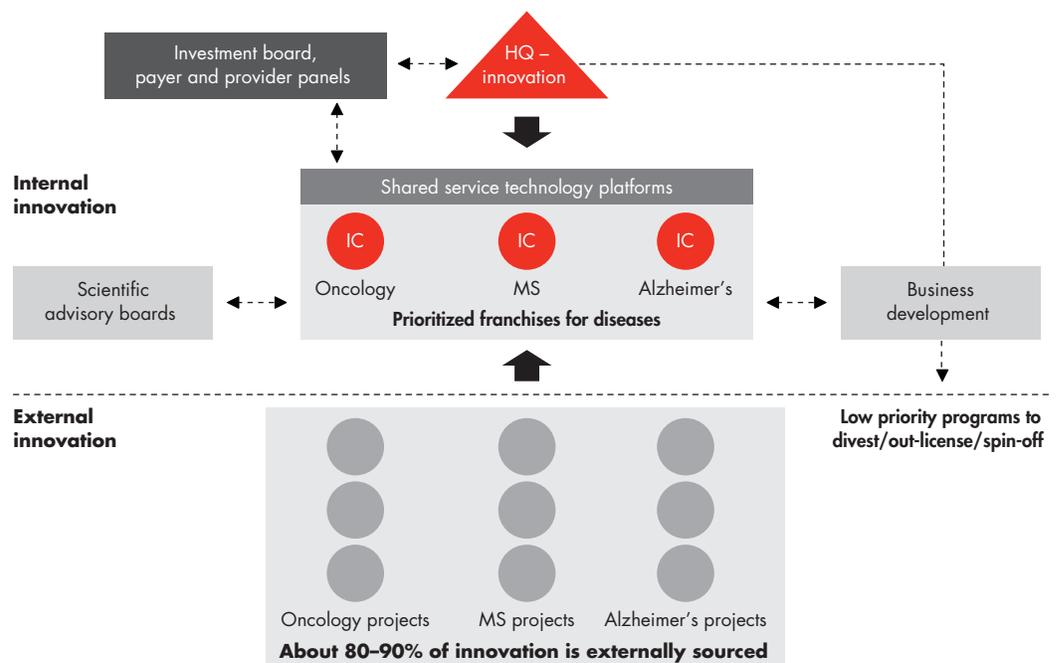
While scale can be an enormous commercial advantage, it can be kryptonite for innovation. That raises a challenge for pharma: Where does a company draw the line? Clearly, scale has a place in pharma development in late stages of development, particularly for very large-scale trials, as well as manufacturing. In fact, any process innovation that is repeatable can be industrialized, not just in later-stage development, but even in early research or areas like medicinal chemistry. Where scale often doesn’t work is in areas of true product innovation, where ingenuity matters. In such instances, pharma companies need milestone-based processes where progress in projects can be reviewed on an individual basis.

To unleash innovation, Big Pharma will need to revisit its singular approach to R&D and differentiate between activities: One, activities that warrant process innovation and two, those that should not be over-engineered but allowed autonomy in order to fuel creativity. Some pharma companies such as Roche have already begun this process by separating research and early-stage development from later-stage development into two organizations.

An emerging new R&D model

Seeking medical differentiation, building flexibility in an organization and revisiting processes to identify the ones best suited for scale versus creativity—each goal is challenging by itself. Taken together, they can radically transform a pharma organization. In practical terms, what would this degree of change entail? While each company will want to find its own unique solution, consider one hypothetical model for a large, innovation-led pharma company (see Figure 2).

Figure 2: New innovation model: Innovation Centers (ICs) with an external focus and a high degree of scientific and entrepreneurial freedom



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At the core of this company's new innovation model are Innovation Centers (ICs) focused on specific therapeutic or disease areas. Depending on the stage of the innovation and the nature of their work, these ICs are based on different criteria such as more internal or external resources; unique milestone or success definitions. The ICs share only a few internal service technology platforms—those that are truly proprietary, like RNA interference—but they have some common characteristics:

- The ability to attract and retain the best talent, especially scientists and innovation managers (two very distinct roles that are often conjoined in today's pharma organizations);
- The expertise to identify and access the best science within their disease area, be it internal or external;
- The ability to conduct limited internal research for validation;
- The allocation of the IC budget among programs, such that there is an adequate balance between the internal and external sources of innovation; and
- The ability to flexibly hire the right staff for specific projects, and maintain very limited permanent staff, mostly functional management. In particular, this fluid organization structure should encourage the creation of more “dual staffing” roles, where academic researchers are invited to work full- or part-time on commercial pharma projects.
- The flexibility to create ICs at a regional or global level, based on ensuring that they attract the best talent, with the right cultural fit.

To make the model work, the pharma company puts in place the right incentives for each IC team. While incentives vary substantially from IC to IC, they are always multi-year, aligned with the specific business plan and linked to milestones.

Just as in biotech, key contributors get significantly rewarded for real success; but instead of being tied arbitrarily to the annual stage/gate processes, their success is measured in NDAs/BLAs² or any other dollar-related exit criteria the company chooses.

ICs are tested on their progress against business plans regularly in a peer review with external scientific advisory boards. The process goes beyond checking off metrics to a more qualitative assessment that asks questions like, “Is the scientific progress strong enough to meet unmet medical needs and is it sufficiently differentiated from alternatives?”

The pharma company's business development team works closely with ICs to enable access to external science. The skill set required for business development requires substantial flexibility in contracting and deal-structuring abilities. Once again, this is about making things happen rather than checking lists for in-licensing criteria. The team drills down on how to maximize the value of assets, identifies low-priority programs to be shed in disease areas that are no longer a priority, and actively nurtures its networks in academia and biotech.

The role of the R&D chief is no longer to coordinate processes in a prescriptive manner for early-stage R&D, but to be a strategic architect and portfolio investor. In concrete terms, the R&D team becomes the organization's headquarters for innovation. It sets the R&D vision and provides strategic direction (which TA/DAs³, underlying biologic mechanisms and new technologies should the pharma company invest in?), objectives (what are the right multi-year goals for the company?) and budget allocation (how do we allocate resources among the various ICs?). While these decisions need to support the overall R&D business case, this is no longer a one-size-fits-all approach with annual throughput (how many programs did you advance into the clinic?), but rather a process similar to venture capital investment in biotechs (in the next round, what are the proof-points we need to continue investing?).

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Those innovation investment decisions are challenged regularly by an investment board that includes internal executives (except those, such as the heads of the ICs, who might have a conflict of interest) as well as outside members. This board provides more than scientific advice—and therefore, includes “customers” such as payers and healthcare providers. They review IC business plans with an eye on return on capital invested and set specific metrics and milestones.

The model pre-supposes the separation of late-stage development (III and IV) into one development organization that spans all therapeutic areas and geographies: a veritable global “innovation marketplace.” This organization takes into account the perspectives of the customer and the market and excels in providing the necessary regulatory proof for the molecules developed by the ICs as quickly and cost-efficiently as possible.

The challenge ahead

We believe Big Pharma can build just such an innovation-led organization—if its leaders have the appetite and patience to embrace change. Like all metamorphosis, transforming a large pharma company will be a slow, sometimes uncomfortable process. Leaders will need to probe deep before embarking on the mission. What are the concrete unmet medical needs the company can target? Which improvements in patient health will justify an attractive price point that governments, payers and patients are willing to pay for? How does the company's proposed solution compare with what is currently available in-house, what the competition is doing and what the R&D team believes is technically feasible in the near future?

The burden will fall on Big Pharma leaders to personally set a new course—even as one hand steadies the helm. In order to be successful, leaders will have to rise above the competition and establish new rules of innovation-led productivity and then get down to the nitty-gritty of transforming the organization. It's a tall order for most organizations, but not

unprecedented. Apple reinvented itself by making a conscious decision to focus on discontinuous products, like the iPod, iPhone and iPad, versus investing in yet another update of the Apple operating system. The company repeatedly outsmarted the industry by successfully challenging the status quo and questioning “how things are done.”

Pharma also requires that level of decisive leadership in order to launch a new era of innovation. For once, the timing couldn't be better. Externally, investors realize pharma innovation needs to be fixed. Currently, they attach little value to discovery and early-stage development in their valuation—and therefore, even in the worst case, the potential negative impact of a new innovation strategy on price-to-earnings ratios is likely to be low. Internally, as in all organizations on the cusp of transformation, employees already know what's not working. They await bold leadership and an inspiring, energizing mission—or at least, for a start, a promise of change. As one executive vice president of R&D says: “The only thing I know for sure is that we can't keep doing the same thing—and expect a better outcome.” 

¹ New molecular entities/biologic license application per dollar of R&D spending

² New drug application/biologic license application

³ Therapeutic area/disease area

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