



Pharma companies can increase innovation—and improve results—through a new approach to R&D

Bringing pharma R&D back to health

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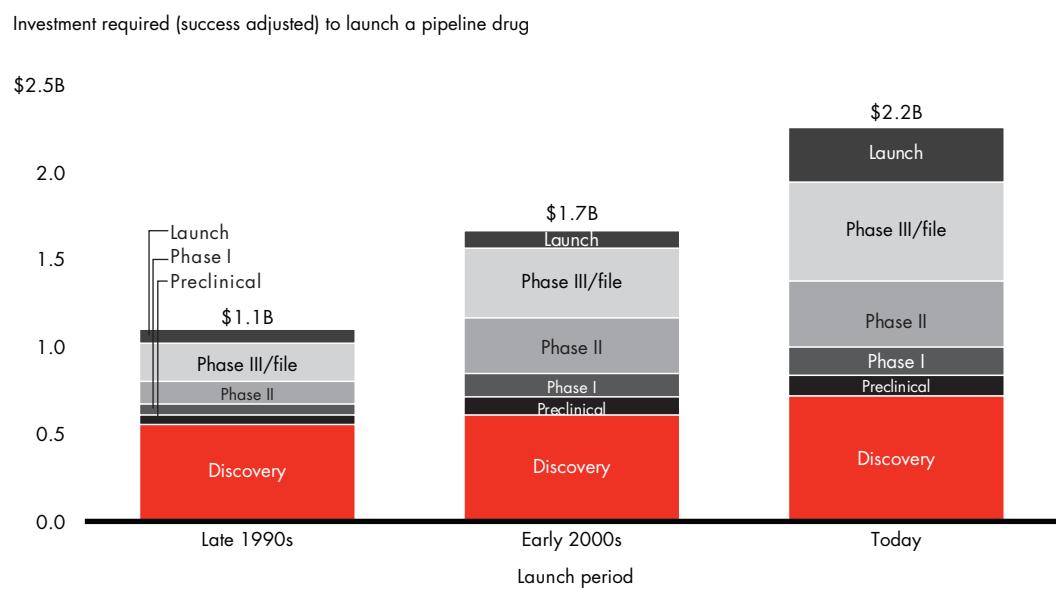
The pharma R&D diagnosis: Underperforming

It's no secret that pharma's traditional approach to R&D is not working. But exactly how broken is it? Bain's drug-economics model shows that the situation is untenable. In the late 1990s, pharma companies spent \$1.1 billion, on average, to develop and launch a new drug. Today, just a decade later, the investment has doubled to \$2.2 billion. (See figure 1.) During this period, R&D productivity, as measured by new molecular entities and biologic license applications per R&D dollar, has declined by 21 percent annually. (See figure 2.) More important, pharma companies have struggled to create value from their investments in innovation. The return on invested capital (ROIC) for new-drug development has dropped from 9 percent in 1995-2000 to an anemic 4 percent today.

Recently, several pharma companies have tried to resuscitate innovation. They have experimented with new R&D organizations, partnerships and technologies. However, no pharma company has truly transformed the traditional R&D approach. Instead, most still rely on scale—more is better—to pursue R&D success. They spend an increasing number of dollars to fund labs and clinics that generate stacks of proprietary knowledge about targets, pathways and compounds. And they still measure success with scale metrics—typically, the number of “shots on goal” that they hope will translate into new products.

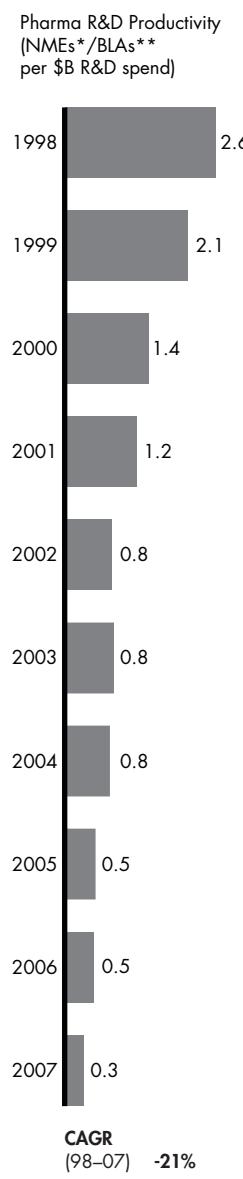
But this scale-based approach to R&D is unsustainable. With blockbuster sales slowing and expected to remain sluggish for the foreseeable future, pharma already feels the economic pinch of weak innovation. Revenues for the top 15 global pharma companies grew by a 10 percent CAGR between 2003 and

Figure 1: Cost of developing a drug



Source: Bain drug economics model, 2008

Figure 2:
Decline in
R&D productivity



*NMEs: New molecular entities
**BLAs: Biologic license applications

Note: NMEs/BLAs approved is measured 5 years after initial R&D investment

Source: EvaluatePharma,
FDA CBER website (PDUFA)

2008, but are expected to drop sharply to just 2 percent over the next four years. (See figure 3.) So, the urgent \$60-billion question (the amount bio-pharma companies spent on R&D in 2007) facing the industry is this: is there a better approach to R&D?

Fortunately, the answer is yes. While success won't be easy given the magnitude of change required and the tough business climate—regulators remain wary of new drugs and payers question reimbursements—change is possible. Despite the hurdles, pharma companies can successfully invest in a new approach to R&D.

Returns-driven R&D: Three steps away

The world needs pharma R&D to succeed. According to the World Health Organization, heart disease, stroke, cancer, chronic respiratory diseases and diabetes cause more than 60 percent of all deaths worldwide. With major health problems still unsolved, pharma companies need to prime their innovation pump and achieve better results.

Step 1: Take the customer's pulse

In R&D, successful results are never guaranteed. But a number of companies, across industries, have found that involving customers early in R&D improves the odds of success. SAP, a worldwide leader in business software, constantly churns out new products for more than 82,000 customers in 25 industries. In 2007, SAP invested almost \$2 billion—nearly 14 percent of its revenues—in R&D at 13 research centers around the globe. SAP involves customers very early in the research process by forming customer advisory boards for each industry segment. Board members are appointed for two-year terms, and they include not just SAP customers but also the competitors' customers. Board members articulate their needs,

and then SAP aligns its R&D priorities to match those needs.

Historically, in pharma, customer-led R&D has not been practiced so rigorously. Pharma companies set R&D priorities based on the opportunity for scientific discovery combined with long-term revenue forecasts—notably, not *profit* forecasts—that promise attractive commercial gains. They seek the customer's input—from physicians, payers and patients—usually only after a product reaches the late-stage pipeline; even then, the feedback influences only launch strategies and market positioning. Moreover, such customer input is heavily focused on physicians, such as the factors that influence their prescriptions. The payer's perspective is largely restricted to reimbursement negotiations. It is rarely an input for setting R&D priorities, and almost never in the early stages of the pipeline—in the labs and clinics. In effect, pharma companies seldom undertake a rigorous assessment of what payers will be willing to pay for—compared with alternative treatments—before deciding what to research.

In the future, pharma companies will need to listen early in their R&D efforts to the voice of customers—especially payers. While a pharma company cannot design products tailored to customer specs, as SAP does, it can guide its R&D closer to customer needs. That shift is imperative. As payers consolidate, they are becoming more powerful and cost conscious, demanding hard evidence that their reimbursement dollars are well spent. By identifying which health outcomes payers are more willing to reimburse, pharma companies can more closely align R&D priorities with market realities. This new approach will be challenging, and even a little frustrating, because payer priorities change over time. But pharma companies must listen, respond and evolve based on what their customers are saying. (See figure 4.)

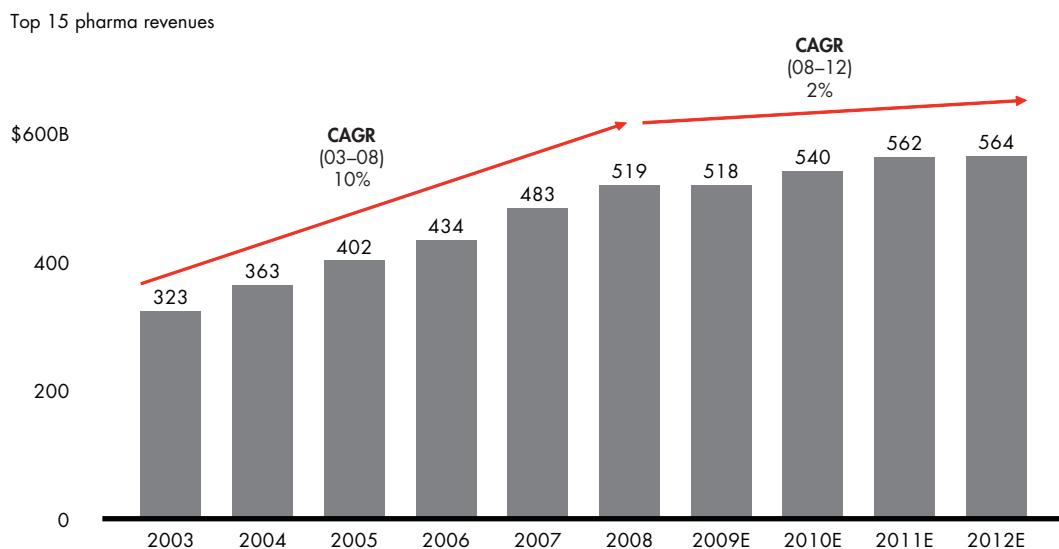
The payoff will be substantial. Pharma companies will have more confidence when funding R&D projects that have passed the payer test—a rigorous evaluation of the improvements in health outcomes that will be valued by payers and are likely to earn attractive reimbursement. From the get-go, these projects will have a greater probability of commercial success despite the alternative treatments available, budget constraints and changing health-care priorities. It will also be easier to stop projects that dip below the bar set by payers, whether on safety, efficacy, or affordability. Pharma companies will find this new approach quite achievable: they already have extensive relationships with payers, as well as deep knowledge of reimbursement systems around the world. It's now a matter of using that payer input early enough to set research priorities.

Novartis is blazing a trail in that regard. It underwent a long and arduous process to get approval in the UK for Lucentis, a wet age-

related macular degeneration treatment. The UK's National Institute for Health and Clinical Excellence (NICE) took two years for an appraisal, including a legal battle when Novartis appealed its initial decision. In the end, a risk-sharing agreement was struck between Novartis and NICE. But Novartis turned that difficult experience into a positive one. In December 2007, even as the legal battle waged, Novartis engaged NICE as a consultant to provide guidance on an upcoming Phase III clinical trial. The "Novartis oor" pilot ensured that Novartis designed better studies, assessed economic value more accurately and laid the groundwork for a smoother NICE appraisal process. Although final results are pending, both Novartis and NICE have praised the collaboration, and Novartis is now talking to national agencies in many countries, including Sweden and the Netherlands, about similar pilots.

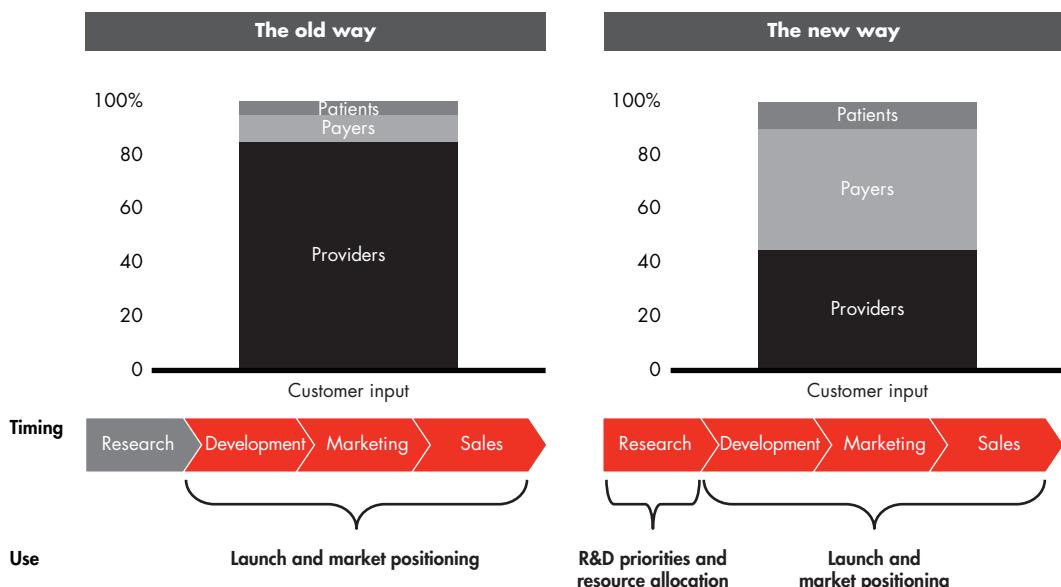
Novartis is actively encouraging payer collaboration. Yet this first step in the new R&D approach

Figure 3: Financial impact from less innovation



Note: Top 15 by pharma revenues, not total revenues
 Source: EvaluatePharma

Figure 4: Step 1: Take the customer's pulse



will require pharma companies to go even further. Successful companies will collaborate with payers earlier than late-stage clinical trials. They will expand the dialogue from single products to a portfolio of products. And they will broaden the mix of payers to reflect a wider range of reimbursement options, including the expanding segment of self-paying patients.

Step 2: Scan for outside innovation

Increasingly, across industries, innovation springs from diverse sources. As a result, leading companies are looking outside their four walls for new ideas to propel growth and stay ahead of the latest innovations. Procter & Gamble (P&G), the world's largest consumer goods products company with 2008 sales of more than \$83 billion and an R&D budget of \$2.2 billion, realized it had a problem when its innovation success rate—the percentage of new products that met financial objectives—stagnated at about 35 percent. The company

prided itself on its R&D prowess—boasting it had more PhDs than the combined science faculties at Harvard, MIT and Stanford and more than 3,800 patents a year to its credit. But clearly, that was not enough. In 2000, P&G adopted a bold approach called “Connect + Develop” to access 50 percent of its innovation from outside the company. It required a major shift in attitude from “not invented here” to “proudly found elsewhere”—and it worked. Today P&G counts its R&D community as 7,500 engineers and scientists inside the organization along with seamless access to 1.5 million outside the organization. By 2006, the company’s innovation success rate had more than doubled, the R&D budget as a percentage of sales had fallen, and about 45 percent of the products under development were based on innovative ideas from outside the company.

Pharma companies, in contrast, too often prefer to look inside their four walls for sources of innovation. Confident they have the best

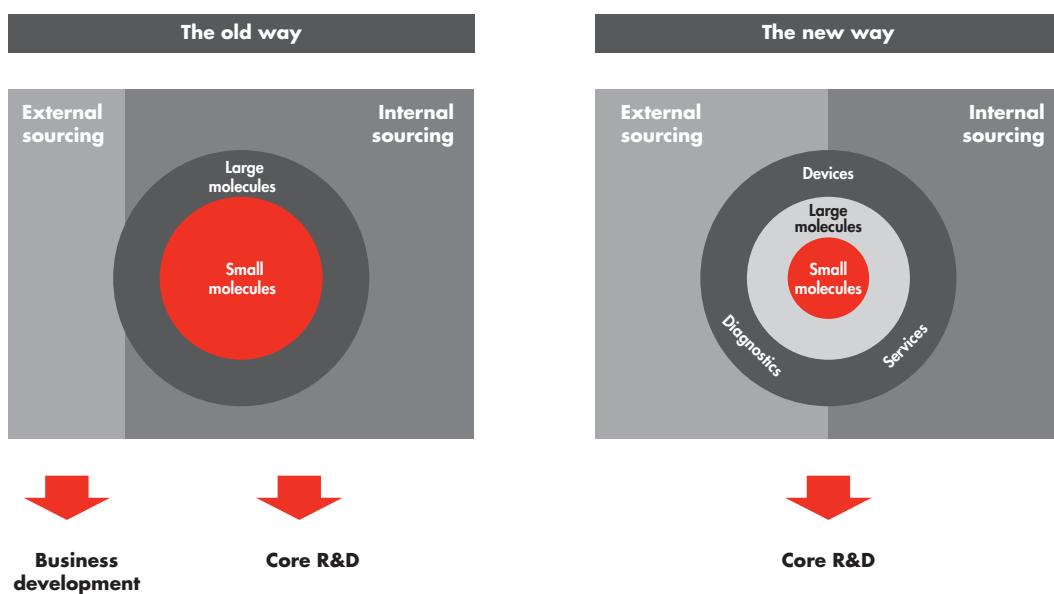
talent and technology inhouse, they rely on themselves to generate new products. To be sure, pharma companies license and acquire a large number of compounds, but the impetus usually comes from business development—often a compulsion to plug gaps in revenue projections. The net result: the full landscape of external innovation is seldom fully evaluated and integrated into pharma's R&D priorities.

For pharma, it's time to eliminate that internal bias. To generate a steady stream of successful new products, pharma companies must throw open their doors and bring home outside innovation. The best scientists always keep tabs on new science; it's part of their DNA. But in this new approach, they need to do more in three ways. One, they must commit to constantly scanning the external landscape with depth and rigor. Two, they must look beyond what's familiar because the future of healthcare will most likely involve a convergence of different treatments. For example,

medical device companies are already testing new products to treat migraines—currently, the domain of drug therapy. What stops a pharma and a medical device company from jointly conducting a clinical trial on a mix of drugs and devices to optimize treatment? Third, and most important, they must act on their insights regarding external science—including stopping internal projects that rank poorly against outside research. Pharma's goal is to improve health outcomes. In the future, it will be even more important to be open-minded about how to get there. (See figure 5.)

Pharma companies can expect significant benefits from objectively scanning outside innovation. Internal R&D projects will be more carefully scrutinized against external alternatives—counter-balancing the cheerleading of internal project teams. Less good money will be thrown after bad because “trailing edge” research projects will be more quickly identified and not as easy to justify. Also, pharma

Figure 5: Step 2: Scan for outside innovation



companies will be able to double down on the most promising R&D projects, whether internal or external. Resources will flow more to whichever sources of innovation appear to have the highest potential for success. This new approach is a major shift in mindset. But, it plays to a pharma company's strength: their teams of top-caliber scientists who have the ability to judge external science. Now, it's time to act on their judgment, even when it means choosing the external over the internal.

GlaxoSmithKline (GSK) is embracing such external innovation. It launched the Center of Excellence for External Drug Discovery (CEEDD) to access "best from anywhere science." By establishing CEEDD, an independently managed group with a dedicated budget, GSK's goal is to put external and internal R&D on the same footing and make objective choices about the most-promising products to fund in late-stage development and commercialization. Eli Lilly is also tapping external innovation. In 2001, it launched InnoCentive as a wholly-owned subsidiary to explore outside solutions to problems identified by its scientists. Doing so proved so successful that by 2006 InnoCentive was spun off as a multi-industry platform to connect "seekers" of R&D problems to "solvers" in a virtual marketplace.

GSK and Eli Lilly are making bold moves to benefit from outside innovation. But to completely embed this second step in the new R&D approach, a pharma company will need to open itself up even more. It must constantly scan outside innovation as a core R&D activity. It will need to widen the lens to include industries such as devices, diagnostics and services. Finally, it will have to fully integrate that information into every R&D investment decision.

Step 3: Act on the right numbers

Private equity firms achieve high returns, or not, based on their ability to make disciplined investment decisions. The top firms succeed repeatedly, not randomly, over long time periods by systematically acquiring companies in specific sectors, increasing their value and exiting at the earliest possible date to achieve their target returns. Success in this approach comes because the management team at the private equity firm is fully aligned on key decisions—which include not acting when the price is not right. The tight link between performance and compensation within the firm reinforces discipline in investment decisions.

Most pharma companies focus on revenues instead of R&D returns. Revenues are relatively easier to project—plug in the patient population, market share and product price, and the formula yields sales. By contrast, projecting returns is far harder because it requires a complete accounting of costs—costs that are sprinkled across separate budgets such as pre-clinical, clinical, regulatory, manufacturing and marketing. It also requires considering opportunity costs: would investing the next R&D dollar earn a higher return elsewhere? With little focus on expected relative returns, pharma companies end up funding undeserving projects too long.

Instead, pharma companies need to employ the same financial rigor as top-tier private equity firms. Both manage large portfolios of assets that must deliver attractive returns over very long cycles, and for both, discipline in investing is the key to success. For pharma, it starts with projecting revenues based on a *realistic* set of assumptions, accounting for a marketplace that is increasingly crowded and shaped by the availability of high quality generics. In addition, it means calculating total costs based on the *entire* length of the project, from the lab

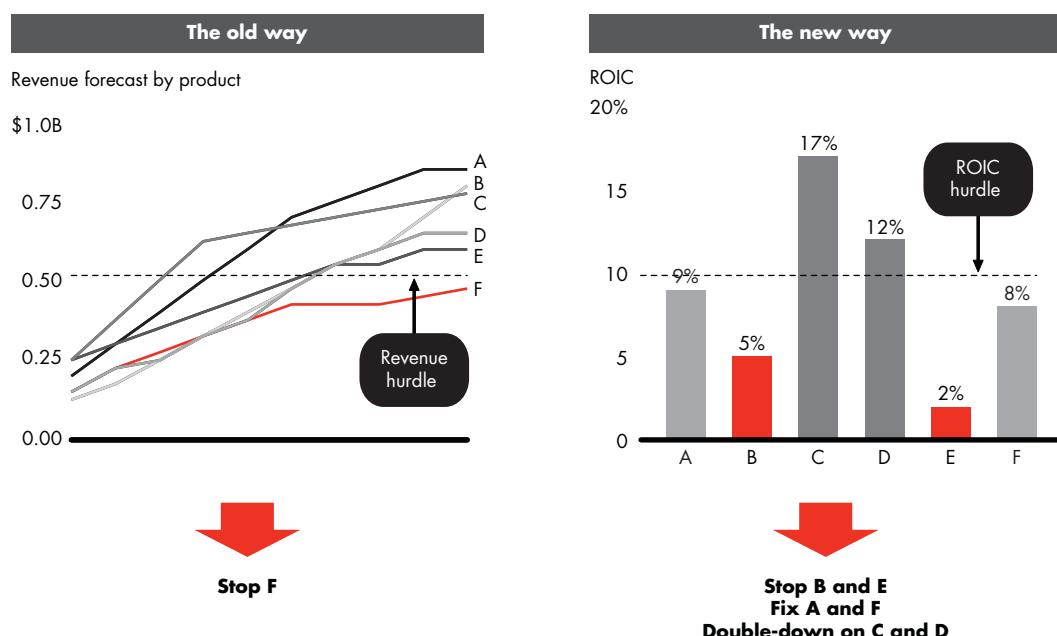
to the marketplace. Such analysis of revenues and costs will yield the expected ROIC and allow R&D decision makers to fund projects against the appropriate hurdle rates. Tracking these hurdles is a constant process: disciplined funding decisions must be made at the outset, but also at every major stage to ensure that dollars are spent only on the most attractive projects. (See figure 6.)

Pharma companies will reap rewards from such financial discipline. For one, this new approach increases the transparency of R&D costs and puts greater pressure on actively reducing them. For another, it leads to a more efficient allocation of resources by turning the capital spigot on and off. In this approach, only the most deserving—not necessarily the most high-profile—projects get funded. Fortunately, pharma companies have the necessary financial sophistication to pursue this returns-based approach. The challenge is calculating the right numbers and acting on them.

AstraZeneca demonstrated such financial discipline recently. Even though the company continues to invest in novel ways to treat gastro-esophageal reflux disease (GERD), it stopped investing in the development of other gastrointestinal drugs. The problem was not revenues—Nexium and Prilosec accounted for more than \$6 billion in sales in 2008—the problem was returns. AstraZeneca felt it was unlikely to discover new and differentiated drugs in that area compared with existing therapies. Instead, it could earn better reimbursement in areas like diabetes and obesity. Using similar logic, Pfizer recently decided to exit cardiovascular R&D.

AstraZeneca and Pfizer exemplify decision making based on the right numbers. This third step in the new R&D approach, though, will require even greater discipline by pharma companies. They will have to apply stringent ROIC hurdles from the outset. Then, they will have to reallocate R&D dollars across projects as value

Figure 6: Step 3: Act on the right numbers



forecasts change. And most important of all: they will have to set a high bar on expected ROIC in order to improve the rate of return from the current lackluster 4 percent.

How to get started

At first sight, focusing single-mindedly on returns-driven R&D might seem a marked departure from the past. But in practice, it builds off existing skills and strengths, and several pharma companies have already begun to experiment with aspects of returns-driven R&D. Fully implementing this new approach will require careful, sequenced implementation of all three steps. A helpful starting point for any pharma company is to review the existing pipeline against three filters:

- *Is each R&D project a priority from the payer's perspective?* To facilitate this exercise, a pharma company can convene a payer panel and subject each pipeline compound to its scrutiny. Non-disclosure agreements will ensure confidentiality and foster a frank discussion about which compounds have the most promising future—as seen through the payer's eyes.
- *Is each R&D project based on the best available science?* This filter requires thoroughly scanning innovation inside and outside the company. To reduce the burden, the pharma company should concentrate only on projects the payer panel found promising. The goal: to identify projects with the strongest scientific merit, regardless of source.
- *Is each R&D project above the ROIC hurdle?* It's time to do the math. For all projects that pass the payer and innovation screens, project teams need to forecast ROIC—taking into account realistic assumptions and total costing. R&D management can then rank and assess the portfolio.

Pharma managers will be surprised how asking these questions quickly leads to clarifying the R&D priorities. Even rough answers will yield a list of potential winners—and laggards. The pharma company will then be able to stop or accelerate projects accordingly. It will also have the opportunity to choose the best plans. For example, by modifying the designs of its trials, a pharma company can deliver clinical data that payers will most value in their reimbursement calculations. R&D leaders will emerge more informed, focused and energized by their effort.

However, a pipeline review is only an initial step. As a follow up, pharma companies will need to invest in new capabilities. While the specifics will vary by company, these capabilities could include setting up a global network of trusted payers to provide input; forming an innovation team to routinely refresh the wide-reaching assessments of external innovation; and creating a financial advisory board to offer disciplined, outside-in views of investment opportunities. Along with new capabilities, pharma companies will need to clarify who makes decisions. Tough calls are central to this new approach, but they won't get made unless it is clear who has the authority to make bold returns-driven decisions.

Successfully transitioning to returns-driven R&D, therefore, will depend on leadership. The right leaders will need to be both “bench scientists” and “business scientists”—possessing the confidence and ability to engage payers, tap outside innovation, and exercise rigorous financial discipline. In turn, their new behaviors will cascade through the R&D organization and catalyze change at all levels. To be sure, every step forward will be challenging—but doing things the old way is no longer an option. Given the low yield of today's drug development, it's time to breathe life back into pharma R&D. 

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